10/014,326

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? ds

Set      Items   Description
S1       77197   T(W)CELL(W)RECEPTOR??
S2       19632   ZIPPER
S3         185   S1 AND S2
S4         158   S3 AND PY<=1998
S5      418046   SOLUBLE
S6          26   S4 AND S5
S7          19   RD (unique items)
S8         245   SOLUBLE(5N) (T(W)CELL(W)RECEPTOR)
S9      356655   LIGAND
S10         47   S8 AND S9
S11         29   RD (unique items)
S12         19   S11 AND PY<=1998
? s mhc
     S13  101598  MHC
? s s8 and s13
              245  S8
           101598  S13
     S14       83  S8 AND S13
? s s14 and py<=1998
Processing
               83  S14
         33643774  PY<=1998
     S15       62  S14 AND PY<=1998
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
     S16       42  RD (unique items)
? s bind? or interact?
Processing
          1934387  BIND?
          1843653  INTERACT?
     S17 3365401  BIND? OR INTERACT?
? s s16 and s17
               42  S16
          3365401  S17
     S18       29  S16 AND S17
? t s18/3,k,ab/1-29

 18/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

11435532   98318213   PMID: 9655481
   Detection of antigen-specific T cells with multivalent soluble class II
MHC covalent peptide complexes.
  Crawford F; Kozono H; White J
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? ds

Set      Items   Description
S1       72576   T(W)CELL(W)RECEPTOR
S2       15773   HETERODIMERI?
S3         340   S1 AND S2
S4      903386   REVIEW
S5          11   S3 AND S4
S6           8   RD (unique items)
? s soluble
      S7  418894  SOLUBLE
? s s3 and s7
             340  S3
          418894  S7
      S8      57  S3 AND S7
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
      S9      40  RD (unique items)
? t s9/3,k,ab/1-40

 9/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

14976739   22340338   PMID: 12454477
   The production, purification and crystallization of a soluble
heterodimeric form of a highly selected T-cell
receptor in its unliganded and liganded state.
  Clements Craig S; Kjer-Nielsen Lars; MacDonald Whitney A; Brooks Andrew G
; Purcell Anthony W; McCluskey James; Rossjohn Jamie
  The Protein Crystallography Unit, Department of Biochemistry and
Molecular Biology, School of Biomedical Sciences, Monash University,
Clayton, Victoria 3168, Australia.
  Acta crystallographica. Section D, Biological crystallography (Denmark)
 Dec 2002, 58 (Pt 12) p2131-4, ISSN 0907-4449 Journal Code: 9305878
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  T-cell antigen receptors (TcRs) are heterodimeric cell-surface
receptors that play a pivotal role in the cellular immune response. The TcR
interacts specifically with a peptide-laden major histocompatability
complex (pMHC). A human TcR has been characterized that interacts with an
immunodominant epitope, FLRGRAYGL, from the Epstein-Barr virus, a
ubiquitous human pathogen, in complex with HLA-B8. Despite the vast TcR
repertoire, this TcR is found in up to 10% of the total T-cell population
in seropositive HLA-B8+ individuals. In this report, this highly selected
TcR is characterized by expressing in Escherichia coli, refolding,
purifying and crystallizing the receptor. In addition, the HLA-B8-FLRGRAYGL
complex has been expressed in E. coli, refolded and shown to be
functionally active. Using native gel electrophoresis, the refolded TcR is
shown to be capable of binding sp
```

Dialog Acc No: 10175454 IFI Acc No: 2002-0119149 IFI Acc No: 2002-0030365
Document Type: C
MULTIVALENT **T CELL RECEPTOR** COMPLEXES; CAN BE USED FOR DELIVERING THERAPEUTIC AGENTS OR FOR DETECTING MAJOR HISTOCOMPATIBILITY COMPLEX (MHC)-PEPTIDE COMPLEXES
Inventors: Boulter Jonathan Michael (GB); Jakobsen Bent Karsten (GB)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020119149 20020829 US 2001912787 20010725
Publication Kind: A1
Division Pub(No),Applic(No,Date): PENDING US 99334969 19990617
Priority Applic(No,Date): GB 98107592 19980519; GB 98211295 19980929; WO 99GB1583 19990519

Abstract: The present invention relates to a synthetic multivalent **T cell receptor** complex for binding to a MHC-peptide complex, which multivalent **T cell receptor** complex comprises a plurality of T cell receptors specific for the MHC-peptide complex. It is preferred that the T cell receptors are refolded recombinant **soluble** T cell receptors. The synthetic multivalent **T cell receptor** complex can be used for delivering therapeutic agents or for detecting MHC-peptide complexes, and methods for such uses are also provided.

MULTIVALENT **T CELL RECEPTOR** COMPLEXES...

Dialog Acc No: 10198684 IFI Acc No: 2002-0142389 IFI Acc No: 2002-0036664
Document Type: C
SOLUBLE T CELL RECEPTOR; RECEPTOR PROTEIN FOR USE AS TOOL IN THE DIAGNOSIS AND TREATMENT OF INFECTION AND AUTOIMMUNE DISEASE
Inventors: Bell John Irving (GB); Boulter Jonathan Michael (GB); Gao George Fu (US); Jakobsen Bent Karsten (GB); Willcox Benjamin Ernest (GB)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020142389 20021003 US 200114326 20011113
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): ABANDONED US 99335087 19990617
Section 371 Pub(No,Date),Applic(No,Date):US 99335087 19990617;WO 99GB1588 19990519
Priority Applic(No,Date): GB 98107592 19980519; GB 98211295 19980929

Abstract: The present invention relates to a recombinant **soluble T cell receptor**. The **T cell receptor** (TCR) is refolded and comprises a recombinant TCR alpha or gamma chain extracellular domain having a first heterologous C-terminal dimerisation peptide; and a recombinant TCR beta or delta chain extracellular domain having a second C-terminal dimerisation peptide which is specifically **heterodimerised** with the first dimerisation peptide to form a **heterodimerisation** domain, which may be a coiled coil domain. The invention also provides nucleic acid sequences encoding the recombinant TCR and a method for producing the recombinant TCR. The TCR may be labelled with a detectable label so as to enable the detection of specific MHC-peptide complexes. Alternatively, it can be linked to a therapeutic agent such as a cytotoxic agent or an immunostimulating agent so as to deliver such an agent to the site of a specific MHC-peptide complex.

9/3,K,AB/28 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03626496 Genuine Article#: PU285 Number of References: 25
Title: A GENERAL-METHOD FOR FACILITATING **HETERODIMERIC** PAIRING BETWEEN 2 PROTEINS - APPLICATION TO EXPRESSION OF ALPHA-T-CELL AND BETA-**T-CELL RECEPTOR** EXTRACELLULAR SEGMENTS (Abstract Available)
Author(s): CHANG HC; BAO ZZ; YAO Y; TSE AGD; GOYARTS EC; MADSEN M; KAWASAKI E; BRAUER PP; SACCHETTINI JC; NATHENSON SG; REINHERZ EL
Corporate Source: HARVARD UNIV,SCH MED,DANA FARBER CANC INST,IMMUNOBIOL LAB,44 BINNEY ST/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT MED/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT PATHOL/BOSTON//MA/02115 ; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT MICROBIOL & IMMUNOL/BRONX//NY/10461; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT BIOCHEM/BRONX//NY/10461; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT CELLBIOL/BRONX//NY/10461; PROCEPT INC/CAMBRIDGE//MA/02139
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 1994, V91, N24 (NOV 22), P11408-11412
ISSN: 0027-8424
Language: ENGLISH Document Type: ARTICLE
Abstract: Generation of **soluble T-cell receptor** (TCR) molecules by a variety of genetic engineering methods has been hampered by inefficient pairing of alpha and beta subunits in the absence of their respective transmembrane regions and associated CD3 components. To overcome this obstacle, we have added 30-amino acid-long segments to the carboxyl termini of alpha and beta extracellular domains via a cleavable flexible linker. These peptide segments (BASE-p1 for alpha and ACID-p1 for beta) have been previously shown to selectively associate to form a stable **heterodimeric** coiled coil termed a leucine zipper. Homodimeric structures are not permitted due to electrostatic repulsion among amino acid side chains. Expression of a representative TCR-leucine zipper fusion protein in a baculovirus expression system results in production of alpha beta TCR heterodimer at 0.6-1.4 mg/liter. This yield is 5- to 10-fold greater than that of the TCR expressed in the absence of the synthetic leucine zipper sequence. The structure of the TCR component of the fusion heterodimer was judged to be native when probed with a panel of 17 mAbs specific for alpha and beta constant and variable domains. A mAb specific for the isolated BASE-p1/ACID-p1 coiled coil was also generated and shown to react with the TCR fusion protein. The above technology should be broadly useful in the efficient production and purification of TCRs as well as other **heterodimeric** proteins.

Title: A GENERAL-METHOD FOR FACILITATING **HETERODIMERIC** PAIRING BETWEEN 2 PROTEINS - APPLICATION TO EXPRESSION OF ALPHA-T-CELL AND BETA-**T-CELL RECEPTOR** EXTRACELLULAR SEGMENTS
Abstract: Generation of **soluble T-cell receptor** (TCR) molecules by a variety of genetic engineering methods has been hampered by inefficient pairing...

...ACID-p1 for beta) have been previously shown to selectively associate to form a stable **heterodimeric** coiled coil termed a leucine zipper. Homodimeric structures are not permitted due to electrostatic repulsion ...

...be broadly useful in the efficient production and purification of TCRs as well as other **heterodimeric** proteins.
...Research Fronts: THE AUTOGRAPHA-CALIFORNICA NUCLEAR POLYHEDROSIS-VIRUS P10 GENE; RECOMBINANT JUVENILE-HORMONE ESTERASE)
92-3772 001 (**T-CELL RECEPTOR**; LPR MICE; EARLY FETAL THYMOCYTES EXPRESSING FC-GAMMA-RII/III CONTAINS PRECURSORS)
92-4628 001 (**T-CELL RECEPTOR** V-BETA GENE USAGE;

SIMILAR MYELIN BASIC-PROTEIN PEPTIDE MAJOR HISTOCOMPATIBILITY COMPLEXES; CHEMICAL DETAILS OF...

9/3,K,AB/29 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03275916 Genuine Article#: NR989 Number of References: 66
Title: B7 AND INTERLEUKIN-12 COOPERATE FOR PROLIFERATION AND INTERFERON-GAMMA PRODUCTION BY MOUSE T-HELPER CLONES THAT ARE UNRESPONSIVE TO B7 COSTIMULATION (Abstract Available)
Author(s): MURPHY EE; TERRES G; MACATONIA SE; HSIEH CS; MATTSON J; LANIER L ; WYSOCKA M; TRINCHIERI G; MURPHY K; OGARRA A
Corporate Source: DNAX RES INST MOLEC & CELLULAR BIOL INC,901 CALIF AVE/PALO ALTO//CA/94304; DNAX RES INST MOLEC & CELLULAR BIOL INC/PALO ALTO//CA/94304; WASHINGTON UNIV,SCH MED,DEPT PATHOL/ST LOUIS//MO/63110; WISTAR INST ANAT & BIOL/PHILADELPHIA//PA/19104
Journal: JOURNAL OF EXPERIMENTAL MEDICINE, 1994, V180, N1 (JUL 1), P223-231
ISSN: 0022-1007
Language: ENGLISH Document Type: ARTICLE
Abstract: We have previously shown that dendritic cells isolated after overnight culture, which can express B7 and are potent stimulators of naive T cell proliferation, are relatively poor at inducing the proliferation of a panel of murine T helper 1 (Th1) clones. Maximal stimulation of Th1 clones was achieved using unseparated splenic antigen presenting cells (APC). An explanation for these findings is provided in the present study where we show that FcR(+) L cells transfected with B7 stimulate minimal proliferation of Th1 clones in response to anti-CDS antibodies, in contrast to induction of significant proliferation of naive T cells. However, addition of interleukin 12 (IL-12) to cultures of Th1 cells stimulated with anti-CDS and FcR(+) B7 transfectants resulted in a very pronounced increase in proliferation and interferon gamma (IFN-gamma) production. Exogenous IL-12 did not affect the B7-induced proliferation of naive T cells. This showed that whereas costimulatory signals delivered via B7-CD28 interaction are sufficient to induce significant proliferation of naive T cells activated through occupancy of the **T cell receptor**, Th1 T cell clones require cooperative costimulation by B7 and IL-12. This costimulation was shown to be specific by inhibition of proliferation and IFN-gamma production using chimeric **soluble** cytolytic T lymphocyte-associated antigen 4-human IgG(1)Fc (CTLA4-Ig) and anti-IL-12 antibodies. Furthermore, the significant antigen specific proliferation and IFN-gamma production by Th1 clones observed when splenocytes were used as APC was almost completely abrogated using CTLA4-Ig and anti-IL-12 antibodies. Thus two costimulatory signals, B7 and IL-12, account for the ability of splenic APC to induce maximal stimulation of Th1 clones. IL-10 downregulates the expression of IL-12 by IFN-gamma-stimulated macrophages and this may account largely for the ability of IL-10 to inhibit APC function of splenic and macrophage APC for the induction of Th1 cell proliferation and IFN-gamma production. Indeed we show that IL-12 can overcome the inhibitory effect of IL-10 for the APC-dependent induction of proliferation and IFN-gamma production by Th1 clones. These results suggest that proliferation by terminally differentiated Th1 clones, in contrast to naive T cells, requires stimulation via membrane-bound B7 and a cytokine, IL-12. It is possible that these signals may result in the activation of unresponsive T cells during an inflammatory response. IL-10, by its role in regulating such innate inflammatory responses, may thus help to maintain these T cells in an unresponsive state.

...Abstract: are sufficient to induce significant proliferation of naive T cells activated through occupancy of the **T cell receptor**, Th1 T cell clones require cooperative costimulation by

B7 and IL-12. This costimulation was shown to be specific by inhibition of proliferation and IFN-gamma production using chimeric **soluble** cytolytic T lymphocyte-associated antigen 4-human IgG(1)Fc (CTLA4-Ig) and anti-IL...
...Identifiers--CELL STIMULATORY FACTOR; LYMPHOCYTE MATURATION FACTOR; NATURAL-KILLER-CELLS; DENDRITIC CELLS; MONOCLONAL-ANTIBODIES; **HETERODIMERIC** CYTOKINE; CD28 PATHWAY; TH1 CELLS; ANTIGEN; EXPRESSION

9/3,K,AB/30 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03189176 Genuine Article#: NM065 Number of References: 75
Title: REGULATION OF THE AVIDITY OF INTEGRIN ALPHA(4)BETA(7) BY THE BETA(7) CYTOPLASMIC DOMAIN (Abstract Available)

4560212 Genuine Article#: TT376 Number of References: 28
Title: STRUCTURAL-ANALYSIS OF GAMMA-DELTA-TCR USING A NOVEL SET OF TCR GAMMA-CHAIN-SPECIFIC AND DELTA-CHAIN-SPECIFIC MONOCLONAL-ANTIBODIES GENERATED AGAINST **SOLUBLE** GAMMA-DELTA-TCR - EVIDENCE FOR A SPECIFIC CONFORMATION ADOPTED BY THE J-DELTA-2 REGION AND FOR A V-DELTA-1 POLYMORPHISM (Abstract Available)
Author(s): ROMAGNE F; PEYRAT MA; LEGET C; DAVODEAU F; HOUDE I; NECKER A; HALLET MM; VIE H; BONNEVILLE M
Corporate Source: INST BIOL,INSERM U211,9 QUAI MONCOUSTA/F-44035 NANTES 01//FRANCE/; INST BIOL,INSERM U211/F-44035 NANTES 01//FRANCE/; IMMUNOTECH SA/F-13288 MARSEILLE//FRANCE/
Journal: JOURNAL OF IMMUNOLOGICAL METHODS, 1996, V189, N1 (JAN 16), P25-36
ISSN: 0022-1759
Language: ENGLISH Document Type: ARTICLE
Abstract: We recently showed that secretion of non-chimeric disulfide-linked human gamma delta TCR ('**soluble**' TCR, sTCR) comprising V gamma 9 and V delta 2 regions could be achieved by simply introducing translational termination codons upstream from the sequences encoding TCR transmembrane region. Here we extended these findings by demonstrating efficient secretion and **heterodimerization** of gamma delta sTCR comprising V gamma 8; V delta 1 and V delta 3 regions, obtained via the same strategy. After immunization against immunoaffinity-purified **soluble** TCR, several hundreds of TCR-specific monoclonal antibodies (mAb) were generated, which fell in at least seven groups. One set of mAb was directed against a V gamma 8-specific epitope. Strikingly, despite the high degree of sequence homology between V gamma 8 and other V gamma I domains, none of these mAb were crossreactive with other members of the V gamma I family. Three other sets of mAbs were shown to recognize delta chains comprising V delta 1, V delta 2 and V delta 3 regions respectively, regardless of their junctional sequence or of the gamma chain to which they were paired. Among the V delta 1-specific mAb, some specifically recognized V delta 1D delta J delta C delta chains while others reacted with both V delta 1 delta J delta C delta and V delta 1J alpha C alpha chains, which suggested V domain conformational alterations induced by the C region. Moreover, reactivity of one V delta 1-specific mAb (#R6.11) was affected by a polymorphic residue located on the predicted CDR4 loop of the V delta region. Two delta chain-specific mAb (#178 and #515) showed a highly unusual reactivity, which was negatively affected by particular V delta and J delta sequences: (i) mAb #515 and #178 recognized all TCR delta chains except those comprising V delta 1 or V delta 2 regions, respectively and (ii) within TCR delta chains carrying 'permissive' V delta regions, none of those comprising the J delta 2 region were recognized by #515 and/or #178 mAbs, which suggested a highly specific conformation adopted by this particular J delta sequence. Apart from its usefulness in TCR structural studies, this novel set of mAb represents an important tool for the characterization and isolation of gamma delta T cells expressing particular combinations of V gamma/V delta regions and for analysis of V alpha/V delta usage by alpha beta T cells. Moreover, since our present data strongly suggest that gamma delta TCR are easier to obtain in a **soluble** form than cup TCR, an efficient strategy for the generation of Ver region-specific mAb might be to immunize with chimeric gamma delta sTCR comprising particular V alpha regions.

...Title: NOVEL SET OF TCR GAMMA-CHAIN-SPECIFIC AND DELTA-CHAIN-SPECIFIC MONOCLONAL-ANTIBODIES GENERATED AGAINST **SOLUBLE** GAMMA-DELTA-TCR - EVIDENCE FOR A SPECIFIC CONFORMATION ADOPTED BY THE J-DELTA-2 REGION...
Abstract: We recently showed that secretion of non-chimeric disulfide-linked human gamma delta TCR ('**soluble**' TCR, sTCR) comprising V gamma 9 and V delta 2 regions could be achieved by...

...sequences encoding TCR transmembrane region. Here we extended these findings by demonstrating efficient secretion and

heterodimerization of gamma delta sTCR comprising V gamma 8; V delta 1 and V delta 3 regions, obtained via the same strategy. After immunization against immunoaffinity-purified **soluble** TCR, several hundreds of TCR-specific monoclonal antibodies (mAb) were generated, which fell in at...

...our present data strongly suggest that gamma delta TCR ar

5408295 Genuine Article#: VX026 Number of References: 48
Title: ASSEMBLY, SPECIFIC BINDING, AND CRYSTALLIZATION OF A HUMAN TCR-ALPHA-BETA WITH AN ANTIGENIC TAX PEPTIDE FROM HUMAN T-LYMPHOTROPIC VIRUS TYPE-1 AND THE CLASS-I MHC MOLECULE HLA-A2 (Abstract Available)
Author(s): GARBOCZI DN; UTZ U; GHOSH P; SETH A; KIM J; VANTIENHOVEN EAE; BIDDISON WE; WILEY DC
Corporate Source: HARVARD UNIV,DEPT MOL & CELLULAR BIOL,7 DIVIN AVE/CAMBRIDGE//MA/02138; HARVARD UNIV,DEPT MOL & CELLULAR BIOL/CAMBRIDGE//MA/02138; HARVARD UNIV,HOWARD HUGHES MED INST/CAMBRIDGE//MA/02138; CLIN RES INST MONTREAL,IMMUNOL LAB/MONTREAL/PQ H2W 1R7/CANADA/; NINCDS,MOL IMMUNOL SECT,NEUROIMMUNOL BRANCH,NIH/BETHESDA//MD/20892; CHILDRENS HOSP,HOWARD HUGHES MED INST,MOL MED LAB/BOSTON//MA/02115
Journal: JOURNAL OF IMMUNOLOGY, 1996, V157, N12 (DEC 15), P5403-5410
ISSN: 0022-1767
Language: ENGLISH Document Type: ARTICLE
Abstract: T lymphocytes use TCR-alpha beta to bind and to recognize complexes of antigenic peptides bound to MHC proteins located at the surface of APCs, We have assembled and crystallized this intercellular complex of TCR/peptide/MHC from **soluble** human TCR-alpha beta and **soluble** peptide/HLA-A2 complexes. The **soluble** TCR-alpha beta binds specifically to its in vivo ligand, the complex of HLA-AZ, and a peptide from the Tax protein of human T lymphotropic virus type 1. The **soluble** TCR also binds in vitro to an altered peptide ligand, which appears to be a partial agonist in T cell assays as determined by its ability to elicit different cytolytic and lymphokine secretion responses, **Heterodimerization** and the antigenic specificity of the TCR do not require its interchain disulfide bond, transmembrane segments, or glycosylations, Crystals of the TCR/peptide/HLA-A2 complex diffract x-rays, providing the means to study in atomic detail the mechanism of Ag-specific cell-cell recognition between T cells and target cells.

9/3,K,AB/18 (Item 6 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

0009292841 BIOSIS NO.: 199497314126
Unique antigen recognition by a herpesvirus-specific TCR-gamma-delta cell
AUTHOR: Sciammas Roger (Reprint); Johnson Raymond M; Sperling Anne I; Brady William; Linsley Peter S; Spear Patricia G; Fitch Frank W; Bluestone Jeffrey A
AUTHOR ADDRESS: Ben May Inst. and Committee on Immunol., Univ. Chicago, MC1089, 5841 S. Maryland Ave., Chicago, IL 60637, USA**USA
JOURNAL: Journal of Immunology 152 (11): p5392-5397 1994 1994
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: TCR-gamma-delta cells, a T cell subset present in the epithelial and lymphoid tissues, have been implicated in viral and bacterial infections. We have identified a TCR-gamma-delta clone (Tg14.4) that, unlike TCR-alpha-beta cells, recognizes a herpes simplex virus type 1 transmembrane glycoprotein, gl, in an MHC class I- and class II-independent fashion. The TCR of Tg14.4 is composed of rearranged V-delta-8 (a V-alpha-2 family member) and V-gamma-1.2 variable genes, a **heterodimeric** pair not previously described. Furthermore, anti-V-alpha-2 mAbs are sufficient to block recognition of the gl ligand. Strikingly, anti-gl Abs also are capable of blocking recognition, a phenomena that is very rare in TCR-alpha-beta Ag recognition. Therefore, to dissect the mechanism involved in this unique form of Ag recognition, we constructed a mutant of gl, glt, that lacks cell surface expression upon transfection into APCs. This form of gl was not sufficient for Ag presentation. In contrast, wild-type gl expressed in the Ag-processing mutant cell, RMA-S, is recognized by Tg14.4, suggesting that gl presentation occurs independently of classical Ag-processing pathways. In fact, through the use of a **soluble** recombinant gl molecule, gl-lg, we show that Tg14.4 can recognize whole, unprocessed gl protein in the absence of any APCs. These results suggest that there exist alternate and novel forms of TCR Ag recognition, and that the TCR-gamma-delta clone, Tg14.4, may represent a novel T cell subset that, during pathogenic challenge, may respond directly to Ags on the surfaces of bacteria and viruses.

...ABSTRACT: 8 (a V-alpha-2 family member) and V-gamma-1.2 variable genes, a **heterodimeric** pair not previously described. Furthermore, anti-V-alpha-2 mAbs are sufficient to block recognition...
...presentation occurs independently of classical Ag-processing pathways. In fact, through the use of a **soluble** recombinant gl molecule, gl-lg, we show that Tg14.4 can recognize whole, unprocessed gl...
DESCRIPTORS:
MISCELLANEOUS TERMS: ...**T CELL RECEPTOR**;

9/3,K,AB/19 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

10307298 Genuine Article#: 511PM Number of References: 90
Title: Adoptive T-cell therapy for the treatment of solid tumours (ABSTRACT AVAILABLE)
Author(s): Knutson KL (REPRINT) ; Almand B; Mankoff DA; Schiffman K; Disis ML
Corporate Source: Univ Washington,Div Oncol,1959 NE Pacif St,HSB BB1321,Box 356527/Seattle//WA/98195 (REPRINT); Univ Washington,Div

Oncol,Seattle//WA/98195; Univ Washington,Div Nucl Med,Seattle//WA/98195
; Univ Washington,Div Oncol,Seattle//WA/98195
Journal: EXPERT OPINION ON BIOLOGICAL THERAPY, 2002, V2, N1 (JAN), P55-66
ISSN: 1471-2598 Publication date: 20020100
Publisher: ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE
FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND
Language: English Document Type: REVIEW

0009399393 BIOSIS NO.: 199497420678
Peripheral T cell receptors alpha-beta and gamma-delta in patients with Hodgkin's lymphoma
AUTHOR: Akan Hamdi (Reprint); Beksac Meral; Aydogdu Ismet; Koc Haluk; Ilhan Osman; Ozcan Muhit
AUTHOR ADDRESS: Ugur Mumcu Sok. 53/7, Buyukesat 06700, Ankara, Turkey** Turkey
JOURNAL: British Journal of Haematology 87 (3): p544-547 1994 1994
ISSN: 0007-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Antigen recognition by T cells is determined by an antigen specific **T cell receptor** (TCR). Two **heterodimeric** TCR structures associated with CD3 have been defined: TCR alpha-beta and TCR gamma-delta. TCR alpha-beta and its function are well described but the role of TCR gamma-delta in normal and lymphoproliferative disorders is not well established. In newly diagnosed or relapsed/refractory Hodgkin's disease (HD), a disease associated with defective T cell functions and increased sIL-2R, we determined levels of seven TCR alpha-beta variable regions (beta-V5(a), beta-V5(b), beta-v6(a), beta-V12(a), alpha-beta-V(a), alpha-V2(a)) and TCR beta-delta by using monoclonal antibodies (MCA). TCR gamma-delta levels did not show any difference, but several variable regions of the TCR alpha-beta differed when groups are compared with each other and the control group.

0013075124 BIOSIS NO.: 200100246963
Polynucleotides encoding molecular complexes which modify immune responses
AUTHOR: Schneck Jonathan; O'Herrin Sean; Lebowitz Michael S (Reprint); Hamad Abdel
AUTHOR ADDRESS: Pikesville, MD, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1239 (5): Oct. 31, 2000 2000
MEDIUM: e-file
PATENT NUMBER: US 6140113 PATENT DATE GRANTED: October 31, 2000 20001031
PATENT CLASSIFICATION: 435-3201 PATENT ASSIGNEE: The Johns Hopkins University PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Polynucleotides encode **soluble**, multivalent molecular complexes which modify immune responses, and host cells comprise such polynucleotides. The molecular complexes comprise extracellular domains of transmembrane **heterodimeric** proteins, particularly **T cell receptor** and major histocompatibility complex proteins, which are covalently linked to the heavy and light chains of immunoglobulin molecules to provide **soluble** multivalent molecular complexes with high affinity for their cognate ligands. The molecular complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

0014016072 BIOSIS NO.: 200200609583
Molecular complexes which modify immune responses
AUTHOR: Schneck Jonathan; O'Herrin Sean (Reprint); Lebowitz Michael S; Hamad Abdel
AUTHOR ADDRESS: Madison, WI, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1263 (1): Oct. 1, 2002 2002
MEDIUM: e-file
PATENT NUMBER: US 6458354 PATENT DATE GRANTED: October 01, 2002 20021001
PATENT CLASSIFICATION: 424-1341 PATENT ASSIGNEE: The Johns Hopkins University PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Extracellular domains of transmembrane **heterodimeric** proteins, particularly **T cell receptor** and major histocompatibility complex proteins, can be covalently linked to the heavy and light chains of immunoglobulin molecules to provide **soluble** multivalent molecular complexes with high affinity for their cognate ligands. The molecular complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

9/3,K,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06882040 91122149 PMID: 1671358

Heterodimeric , disulfide-linked alpha/beta T cell receptors in solution.

Slanetz A E; Bothwell A L

Department of Biology, Yale University School of Medicine, New Haven, CT 06510.

European journal of immunology (GERMANY) Jan 1991, 21 (1) p179-83, ISSN 0014-2980 Journal Code: 1273201

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Structural and functional analysis of **T cell receptor** (TcR)-ligand binding would be greatly advanced by the availability of an intact, assembled TcR in **soluble** form. We have produced such a molecule, by splicing the extracellular domains of a TcR to the glycosyl phosphatidylinositol membrane anchor sequences of Thy-1. The molecule is expressed in the absence of CD3 on the cell surface, and can be cleaved from the membrane by treatment with phosphatidylinositol-specific phospholipase C. The alpha and beta chains of the **soluble** molecule are paired in the native conformation as judged by reactivity with the anti-V beta 8 monoclonal antibody F23.1, and with the anti-clonotypic monoclonal antibody 1B2; it is a disulfide-linked dimer with a mol. mass of 95 kDa on sodium dodecyl sulfate-polyacrylamide gel electrophoresis under nonreducing conditions, and 47 kDa after reduction. We conclude that we have generated an alpha/beta TcR in **soluble** form.

779151 20060993 PMID: 10595544

Production of **soluble** alphabeta **T-cell receptor** heterodimers suitable for biophysical analysis of ligand binding.

Willcox B E; Gao G F; Wyer J R; O'Callaghan C A; Boulter J M; Jones E Y; van der Merwe P A; Bell J I; Jakobsen B K

MRC Human Immunology Unit, Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, United Kingdom.

Protein science - a publication of the Protein Society (UNITED STATES) Nov 1999, 8 (11) p2418-23, ISSN 0961-8368 Journal Code: 9211750

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A method to produce alphabeta T-cell receptors (TCRs) in a **soluble** form suitable for biophysical analysis was devised involving in vitro refolding of a TCR fusion protein. Polypeptides corresponding to the variable and constant domains of each chain of a human and a murine receptor, fused to a coiled coil **heterodimerization** motif from either c-Jun (alpha) or v-Fos (beta), were overexpressed separately in Escherichia coli. Following recovery from inclusion bodies, the two chains of each receptor were denatured, and then refolded together in the presence of denaturants. For the human receptor, which is specific for the immunodominant influenza A HLA-A2-restricted matrix epitope (M58-66), a **heterodimeric** protein was purified in milligram yields and found to be homogeneous, monomeric, antibody-reactive, and stable at concentrations lower than 1 microM. Using similar procedures, analogous results were obtained with a murine receptor specific for an influenza nucleoprotein epitope (366-374) restricted by H2-Db. Production of these receptors has facilitated a detailed analysis of viral peptide-Major Histocompatibility Complex (peptide-MHC) engagement by the TCR using both surface plasmon resonance (SPR) and, in the case of the human TCR, isothermal titration calorimetry (ITC) (Willcox et al., 1999)[0]. The recombinant methods described should enable a wide range of TCR-peptide-MHC interactions to be studied and may also have implications for the production of other **heterodimeric** receptor molecules.

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09149158 20451136 PMID: 10993731
Heterodimeric CD3epsilongamma extracellular domain fragments: production, purification and structural analysis.
Kim K S; Sun Z Y; Wagner G; Reinherz E L
Laboratory of Immunobiology, Dana-Farber Cancer Institute and Department of Medicine, Boston, MA, 02115, USA.
Journal of molecular biology (ENGLAND) Sep 29 2000, 302 (4) p899-916 , ISSN 0022-2836 Journal Code: 2985088R
Contract/Grant No.: AI19807; AI; NIAID; AI37581; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The CD3 polypeptides (epsilon, gamma, and delta) are non-covalently associated signaling subunits of the **T cell receptor** which form non-disulfide linked epsilongamma and epsilondelta heterodimers. With the goal of investigating their structure, Escherichia coli expression was utilized to produce CD3 ectodomain fragments including the murine CD3epsilon subunit N-terminal Ig-like extracellular domain alone or as a single chain construct with that of CD3gamma. The latter links the CD3gamma segment to the C terminus of the CD3epsilon segment via a 26 amino acid peptide (scCD3epsilongamma26). Although CD3epsilon could be produced at high yield when directed to inclusion bodies, the refolded monomeric CD3epsilon was not native as judged by monoclonal antibody binding using surface plasmon resonance and was largely unstructured by (15)N-(1)H two-dimensional NMR analysis. In contrast, scCD3epsilongamma26 could be refolded readily into a native state as shown by CD, NMR and mAb reactivity. The linker length between CD3epsilon and CD3gamma is critical since scCD3epsilongamma16 containing a 16 residue connector failed to generate a stable heterodimer. Collectively, the results demonstrate that: (i) **soluble heterodimeric** fragments of CD3 can be produced; (ii) cotranslation of CD3 chains insures proper folding even in the absence of the conserved ectodomain stalk region (CxxCxE); and (iii) CD3epsilon has a more stable tertiary protein fold than CD3gamma. Copyright 2000 Academic Press.

Heterodimeric CD3epsilongamma extracellular domain fragments: production, purification and structural analysis.
The CD3 polypeptides (epsilon, gamma, and delta) are non-covalently associated signaling subunits of the **T cell receptor** which form non-disulfide linked epsilongamma and epsilondelta heterodimers. With the goal of investigating their...
... 16 residue connector failed to generate a stable heterodimer. Collectively, the results demonstrate that: (i) **soluble heterodimeric** fragments of CD3 can be produced; (ii) cotranslation of CD3 chains insures proper folding even...

9/3,K,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08779151 20060993 PMID: 10595544
Production of **soluble** alphabeta **T-cell receptor** heterodimers suitable for biophysical analysis of ligand binding.
Willcox B E; Gao G F; Wyer J R; O'Callaghan C A; Boulter J M; Jones E Y; van der Merwe P A; Bell J I; Jakobsen B K
MRC Human Immunology Unit, Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, United Kingdom.
Protein science - a publication of the Protein Society (UNITED STATES) Nov 1999, 8 (11) p2418-23, ISSN 0961-8368 Journal Code: 9211750
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A method to produce alphabeta T-cell receptors (TCRs) in a **soluble** form suitable for biophysical analysis was devised involving in vitro refolding of a TCR fusion protein. Polypeptides corresponding to the variable and constant domains of each chain of a human and a murine receptor, fused to a coiled coil **heterodimerization** motif from either c-Jun (alpha) or v-Fos (beta), were overexpressed separately in Escherichia coli. Following recovery from inclusion bodies, the two chains of each receptor were denatured, and then refolded together in the presence of denaturants. For the human receptor, which is specific for the immunodominant influenza A HLA-A2-restricted matrix epitope (M58-66), a **heterodimeric** protein was purified in milligram yields and found to be homogeneous, monomeric, antibody-reactive, and stable at concentrations lower than 1 microM. Using similar procedures, analogous results were obtained with a murine receptor specific for an influenza nucleoprotein epitope (366-374) restricted by H2-Db. Production of these receptors has facilitated a detailed analysis of viral peptide-Major Histocompatibility Complex (peptide-MHC) engagement by the TCR using both surface plasmon resonance (SPR) and, in the case of the human TCR, isothermal titration calorimetry (ITC) (Willcox et al., 1999). The recombinant methods described should enable a wide range of TCR-peptide-MHC interactions to be studied and may also have implications for the production of other **heterodimeric** receptor molecules.

Production of **soluble** alphabeta **T-cell receptor** heterodimers suitable for biophysical analysis of ligand binding.

A method to produce alphabeta T-cell receptors (TCRs) in a **soluble** form suitable for biophysical analysis was devised involving in vitro refolding of a TCR fusion...

...of each chain of a human and a murine receptor, fused to a coiled coil **heterodimerization** motif from either c-Jun (alpha) or v-Fos (beta), were overexpressed separately in Escherichia...

... is specific for the immunodominant influenza A HLA-A2-restricted matrix epitope (M58-66), a **heterodimeric** protein was purified in milligram yields and found to be homogeneous, monomeric, antibody-reactive, and...

... MHC interactions to be studied and may also have implications for the production of other **heterodimeric** receptor molecules.

9/3,K,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08597414 95285731 PMID: 7768153

Primitive vertebrate immunity: what is the evolutionary derivative of molecules that define the adaptive immune system?

Flajnik M F
Department of Microbiology and Immunology, University of Miami, FL 33136, USA.

Ciba Foundation symposium (NETHERLANDS) 1994, 186 p224-32; discussion 233-6, ISSN 0300-5208 Journal Code: 0356636
Contract/Grant No.: AI27877; AI; NIAID; RR06603; RR; NCRR
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The adaptive immune system is capable of responding to an infinite number of antigens with the antigen-specific receptors immunoglobulin (Ig) and the **T cell receptor** (TCR). Ig binds **soluble** antigens

while TCR recognizes antigen bound in clefts of polymorphic self-encoded major histocompatibility complex (MHC) class I and cla

14976739 22340338 PMID: 12454477

The production, purification and crystallization of a **soluble heterodimeric** form of a highly selected **T-cell receptor** in its unliganded and liganded state.

Clements Craig S; Kjer-Nielsen Lars; MacDonald Whitney A; Brooks Andrew G ; Purcell Anthony W; McCluskey James; Rossjohn Jamie

The Protein Crystallography Unit, Department of Biochemistry and Molecular Biology, School of Biomedical Sciences, Monash University, Clayton, Victoria 3168, Australia.

Acta crystallographica. Section D, Biological crystallography (Denmark) Dec 2002, 58 (Pt 12) p2131-4, ISSN 0907-4449 Journal Code: 9305878

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

T-cell antigen receptors (TcRs) are **heterodimeric** cell-surface receptors that play a pivotal role in the cellular immune response. The TcR interacts specifically with a peptide-laden major histocompatability complex (pMHC). A human TcR has been characterized that interacts with an immunodominant epitope, FLRGRAYGL, from the Epstein-Barr virus, a ubiquitous human pathogen, in complex with HLA-B8. Despite the vast TcR repertoire, this TcR is found in up to 10% of the total T-cell population in seropositive HLA-B8+ individuals. In this report, this highly selected TcR is characterized by expressing in Escherichia coli, refolding, purifying and crystallizing the receptor. In addition, the HLA-B8-FLRGRAYGL complex has been expressed in E. coli, refolded and shown to be functionally active. Using native gel electrophoresis, the refolded TcR is shown to be capable of binding specifically to the refolded HLA-B8-FLRGRAYGL and this TcR has been crystallized in complex with the pMHC. The crystals of the unliganded and liganded TcR diffract to 1.5 and 2.5 A, respectively.

The production, purification and crystallization of a **soluble heterodimeric** form of a highly selected **T-cell receptor** in its unliganded and liganded state.

9/3,K,AB/40 (Item 8 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2948062 IFI Acc No: 9806179
Document Type: C
PRODUCTION OF SUBUNITS OF **SOLUBLE** T CELL RECEPTORS BY CO-TRANSFECTION
Inventors: Bonneville Marc (FR)
Assignee: Immunotech FR; Institut National de la Sante et de la Recherche Medicale FR
Assignee Code: 16381 42342
Publication (No,Date), Applic (No,Date):
US 5723309 19980303 US 94256964 19940914
Publication Kind: A
Calculated Expiration: 20150303
PCT Pub(No,Date),Applic(No,Date): WO 9412648 19940609 WO 93FR1165 19931125
Section 371: 19940914
Section 102(e):19940914
Priority Applic(No,Date): FR 9214203 19921125

Abstract: **Soluble**, single chain T cell receptors, nucleic acid sequences, particularly DNA sequences, encoding the **soluble**, single chain **T cell receptor**, expression vectors containing the DNA sequences, and host cells containing the expression vectors.

PRODUCTION OF SUBUNITS OF **SOLUBLE** T CELL RECEPTORS BY CO-TRANSFECTION

Abstract: **Soluble**, single chain T cell receptors, nucleic acid sequences, particularly DNA sequences, encoding the **soluble**, single chain **T cell receptor**, expression vectors containing the DNA sequences, and host cells containing the expression vectors.

Exemplary Claim: D R A W I N G

1. Process for producing **soluble** T receptors, comprising cotransfecting into a host cell DNA sequences each encoding only a single...

Non-exemplary Claims: 2. Process according to claim 1, wherein V Alpha C/60 /V Beta C Beta **soluble** T receptors are produced by co-transfecting, into a host cell, said DNA sequences each...

...3. Process according to claim 1, wherein V gamma C gamma /V delta C delta **soluble** T receptors are produced by co-transfecting, into a host cell, said DNA sequences each...

...4. Process according to claim 1, wherein V Alpha C/65 /V Beta C delta **heterodimeric soluble** T receptors are produced, in which the constituent subunits are associated via a covalent bond...

...5. Process according to claim 1, wherein V Alpha C delta /V Beta C/65 **heterodimeric soluble** T receptors are produced, in which the constituent subunits are associated via a covalent bond...

...Process according to claim 1, wherein V gamma C gamma /V Alpha C delta hybrid **soluble** T receptors are produced by co-transfecting, into a host cell, a said DNA sequence...

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$3.15 15 Type(s) in Format 4 (UDF)
$3.15 15 Types

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   $156.15  Estimated total session cost   3.286 DialUnits
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Dialog Acc No: 3343591 IFI Acc No: 0019752
Document Type: C
SOLUBLE T CELL RECEPTORS; MEMBRANE-FREE **HETERODIMERIC**, DISULFIDE LINKED ALPHA/BETA **SOLUBLE T CELL RECEPTOR** SHARING A CLONOTYPIC EPITOPE WITH A NATIVE RECEPTOR; FOR SCREENING LIGANDS; FOR IMMUNOSUPPRESSANTS AND THERAPY FOR AUTOIMMUNE DISEASES
Inventors: Bothwell Alfred L M (US); Slanetz Alfred E (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 6080840 20000627 US 95393157 19950217
Publication Kind: A
Calculated Expiration: 20170627
Continuation Pub(No),Applic(No,Date): ABANDONED US 92822538 19920117
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED US 93168782 19931214
Priority Applic(No,Date): US 95393157 19950217; US 92822538 19920117; US 93168782 19931214

Abstract: An intact, assembled **T cell receptor** (TcR) in **soluble** form is provided. The **soluble** TcR is prepared by splicing the extracellular domains of a **T cell receptor** to the glycosyl phosphatidylinositol (GPI) membrane anchor sequences of Thy-1. The molecule is expressed in the absence of CD3 on the cell surface, and can be cleaved from the membrane by treatment with phosphatidylinositol specific phospholipase C (PI-PLC). The alpha and beta chains of the **soluble** molecule are paired in the native conformation as judged by reactivity with the anti-V beta 8 monoclonal antibody F23.1, and with the anti-clonotypic monoclonal antibody 1B2. The **soluble** TcR is a disulfide linked dimer with a molecular mass of 95 kDa on SDS-PAGE under nonreducing conditions, and 47 kDa after reduction.

SOLUBLE T CELL RECEPTORS...

Dialog Acc No: 3409072 IFI Acc No: 0036169
Document Type: C
POLYNUCLEOTIDES ENCODING MOLECULAR COMPLEXES WHICH MODIFY IMMUNE RESPONSES; NUCLEOTIDE SEQUENCES WHICH CODES AN IMMUNOGLOBULIN FUSION PROTEIN; FOR THE DETECTION AND TREATMENT OF ALLERGIES, AUTOIMMUNE DISEASES, TUMORS, INFECTIONS, AND TRANSPLANT EJECTION; ANTITUMOR AGENTS
Inventors: Hamad Abdel (US); Lebowitz Michael S (US); O'Herrin Sean (US); Schneck Jonathan (US)
Assignee: Johns Hopkins University
Assignee Code: 39884
Publication (No,Date), Applic (No,Date):
US 6140113 20001031 US 9863276 19980421
Publication Kind: A
Calculated Expiration: 20170328
Cont.-in-part Pub(No),Applic(No,Date): US 6015884 US 97828712 19970328
Priority Applic(No,Date): US 9863276 19980421; US 97828712 19970328

Abstract: Polynucleotides encode **soluble**, multivalent molecular complexes which modify immune responses, and host cells comprise such polynucleotides. The molecular complexes comprise extracellular domains of transmembrane **heterodimeric** proteins, particularly **T cell receptor** and major histocompatibility complex proteins, which are covalently linked to the heavy and light chains of immunoglobulin molecules to provide **soluble** multivalent molecular complexes with high affinity for their cognate ligands. The molecular complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

Dialog Acc No: 3760508 IFI Acc No: 0235137
Document Type: C
MOLECULAR COMPLEXES WHICH MODIFY IMMUNE RESPONSES
Inventors: Hamad Abdel (US); Lebowitz Michael S (US); O'Herrin Sean (US); Schneck Jonathan (US)
Assignee: Johns Hopkins University
Assignee Code: 39884
Publication (No,Date), Applic (No,Date):
US 6458354 20021001 US 2000668143 20000925
Publication Kind: B
Calculated Expiration: 20170328
Cont.-in-part Pub(No),Applic(No,Date): Pending US 97828712 19970328; US 6140113 US 9863276 19980421; Pending US 99324782 19990603
Priority Applic(No,Date): US 2000668143 20000925; US 97828712 19970328; US 9863276 19980421; US 99324782 19990603

Abstract: Extracellular domains of transmembrane **heterodimeric** proteins, particularly **T cell receptor** and major histocompatibility complex proteins, can be covalently linked to the heavy and light chains of immunoglobulin molecules to provide **soluble** multivalent molecular complexes with high affinity for their cognate ligands. The molecular complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

Abstract: Extracellular domains of transmembrane **heterodimeric** proteins, particularly **T cell receptor** and major histocompatibility complex proteins, can be covalently linked to the heavy and light chains of immunoglobulin molecules to provide **solu**

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2004/Jan W3
         (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
  File  55:Biosis Previews(R)  1993-2004/Jan W3
         (c) 2004 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci  1990-2004/Jan W3
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*File  34: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES 34.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
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*File 434: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES434.
  File 340:CLAIMS(R)/US Patent  1950-04/Jan 22
         (c) 2004 IFI/CLAIMS(R)
*File 340: Annual reload and classification updates delayed due
 to processing issues.

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         1635074  RECEPTOR
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? s extracellular
      S2  409838  EXTRACELLULAR
? s s1 and s2
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          409838  S2
      S3    2225  S1 AND S2
? s disulfide
      S4   75966  DISULFIDE
? s s3 and s4
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           75966  S4
      S5      75  S3 AND S4
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...completed examining records
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? s unstable
      S7  119752  UNSTABLE
? s s6 and s7
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? s fold?
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? t s10/3,k,ab/1-12

 10/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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11705318 99141420 PMID: 9917415

Folding, heterodimeric association and specific peptide recognition of a murine alphabeta **T-cell receptor** expressed in Escherichia coli.

Pecorari F; Tissot A C; Pluckthun A

Biochemisches Institut, Universitat Zurich, Winterthurerstr. 190, Zurich, CH-8057, Switzerland.

Journal of molecular biology (ENGLAND) Jan 29 1999, 285 (4) p1831-43 , ISSN 0022-2836 Journal Code: 2985088R

Document type: Journal Article

03033194 Genuine Article#: MX149 Number of References: 50
Title: T-CELL ANTIGEN RECEPTOR EXPRESSION STUDIED USING SOMATIC-CELL MUTANTS (Abstract Available)
Author(s): CASPARBAUGUIL S; ARNAUD J; RUBIN B
Corporate Source: CHU PURPAN,CRPG,IMMUNOL CELLULAIRE & MOLEC LAB,CNRS/F-31300 TOULOUSE//FRANCE/; CHU PURPAN,CRPG,IMMUNOL CELLULAIRE & MOLEC LAB,CNRS/F-31300 TOULOUSE//FRANCE/
Journal: COMPTES RENDUS DE L ACADEMIE DES SCIENCES SERIE III-SCIENCES DE LA VIE-LIFE SCIENCES, 1994, V317, N1 (JAN), P77-84
ISSN: 0764-4469
Language: FRENCH Document Type: ARTICLE
Abstract: T lymphocytes express membrane antigen receptor TcR/CD3 complexes only when all subunits are correctly assembled. Studies on TcR/CD3 membrane negative T cell variants containing all necessary subunits intracellularly, may allow to identify amino acid important for different subunit interactions. In this review, we summarize our recent work on TcR/CD3 negative variants of the human T cell line Jurkat. We found two critical amino acid in the TcR-alpha and TcR-beta **extracellular** constant regions (phenylalanine n degrees 216 and intrachain **disulfide** cysteine n degrees 212) involved in TcR-alpha beta/CD3-gamma epsilon,delta epsilon intermediary complex/zeta(2) homodimer interactions: (I) amino acid exchanges of phenylalanine demonstrated the importance of an aromatic amino acid residue at this position; (2) the intrachain **disulfide** bond assures a tertiary structure of the constant domain that is necessary for association with zeta(2) homodimers.

...Abstract: line Jurkat. We found two critical a

04567474 Genuine Article#: TU126 Number of References: 19
Title: CONFORMATION OF THE T-CELL ANTIGEN RECEPTOR-BETA CHAIN C-DOMAIN CONTRIBUTES TO V-BETA(3) EPITOPE RECOGNITION BY MONOCLONAL-ANTIBODY KJ25 (Abstract Available)
Author(s): LI ZG; KEMP O; LONGHURST T; MANOLIOS N
Corporate Source: ROYAL N SHORE HOSP,DEPT RHEUMATOL/SYDNEY/NSW 2065/AUSTRALIA/; ROYAL N SHORE HOSP,DEPT RHEUMATOL/SYDNEY/NSW 2065/AUSTRALIA/; UNIV SYDNEY,DEPT MED/SYDNEY/NSW 2065/AUSTRALIA/; UNIV TECHNOL SYDNEY,DEPT MOLEC & CELL BIOL,IMMUNOL UNIT/SYDNEY/NSW 2007/AUSTRALIA/
Journal: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, 1996, V43, N2 (FEB), P140-145
ISSN: 0300-9475
Language: ENGLISH Document Type: ARTICLE
Abstract: The clonotypic T-cell antigen receptor (TCR)-beta chain contains two **extracellular** intrachain **disulfide** bonds. It belongs to the immunoglobulin gene superfamily and is subdivided into variable (V), joining (J), diversity (D) and constant (C) region. Monoclonal antibody (MoAb) KJ25 is believed to recognize an epitope in the V-domain of TCR-beta (V beta(3)) chain, but its epitope requirements are unknown. In this study of TCR-alpha beta chain interactions using chimeric recombinant TCR-beta chains, the authors found that partial substitution of the C beta-domain with that of interleukin-2 receptor a chain (Tac) sequences led to the loss of TCR-V beta(3) epitope recognition by KJ25. These results suggest that epitope recognition of the TCR-V beta(3) by KJ25 MoAb is dependent not only on the V-domain, but also on the close contact with the **extracellular** C-domain which influences the conformation and epitope recognition of the V beta(3)-region. This may not be unique to V beta(3) and may be a general feature of TCR-beta protein **folding**.

Abstract: The clonotypic T-cell antigen receptor (TCR)-beta chain contains two **extracellular** intrachain **disulfide** bonds. It belongs to the immunoglobulin gene superfamily and is subdivided into variable (V), joining...

8330262 95018232 PMID: 7932722

Correctly **folded T-cell receptor** fragments in the periplasm of Escherichia coli. Influence of **folding** catalysts.

Wulfing C; Pluckthun A

Max-Planck-Institut fur Biochemie, Protein Engineering Group, Martinsried, Germany.

Journal of molecular biology (ENGLAND) Oct 7 1994, 242 (5) p655-69, ISSN 0022-2836 Journal Code: 2985088R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The **T-cell receptor** is the central recognition molecule in cellular immunity. Its **extracellular** domains are homologous with and thought to be structurally similar to an antibody Fab fragment. Despite the biological importance of the TCR and the ease of bacterial expression of antibody fragments, there are only few reports of TCR-fragment expression in E. coli. In order to understand the difficulties of expressing correctly **folded** TCR fragments in E. coli, we have characterized the expression behavior of single-chain Fv analogs of three different TCRs (scTCR). All of them can be **folded** into the correct conformation in the periplasm of E. coli, yet the extent of correct **folding** varies greatly. In order to overcome the **folding** problems of some of the scTCRs, we have developed a system with enhanced in vivo **folding** capability based on the simultaneous induction of the heat-shock response and over-expression of the E. coli **disulfide** isomerase DsbA at low temperature. We present a model describing the **folding** of the scTCRs in the periplasm of E. coli and possible points of **folding** assistance. The role of the periplasm as an independent **folding** compartment is emphasized and the existence of a general periplasmic chaperone is postulated. We have also shown that a bivalent scTCR, dimerized in vivo with helix-turn-helix modules, can be expressed in a correctly **folded** form.

Correctly **folded T-cell receptor** fragments in the

09149158 20451136 PMID: 10993731

Heterodimeric CD3epsilongamma **extracellular** domain fragments: production, purification and structural analysis.

Kim K S; Sun Z Y; Wagner G; Reinherz E L
Laboratory of Immunobiology, Dana-Farber Cancer Institute and Department of Medicine, Boston, MA, 02115, USA.

Journal of molecular biology (ENGLAND) Sep 29 2000, 302 (4) p899-916 , ISSN 0022-2836 Journal Code: 2985088R
Contract/Grant No.: AI19807; AI; NIAID; AI37581; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The CD3 polypeptides (epsilon, gamma, and delta) are non-covalently associated signaling subunits of the **T cell receptor** which form non-**disulfide** linked epsilongamma and epsilondelta heterodimers. With the goal of investigating their structure, Escherichia coli expression was utilized to produce CD3 ectodomain fragments including the murine CD3epsilon subunit N-terminal Ig-like **extracellular** domain alone or as a single chain construct with that of CD3gamma. The latter links the CD3gamma segment to the C terminus of the CD3epsilon segment via a 26 amino acid peptide (scCD3epsilongamma26). Although CD3epsilon could be produced at high yield when directed to inclusion bodies, the refolded monomeric CD3epsilon was not native as judged by monoclonal antibody binding using surface plasmon resonance and was largely unstructured by (15)N-(1)H two-dimensional NMR analysis. In contrast, scCD3epsilongamma26 could be refolded readily into a native state as shown by CD, NMR and mAb reactivity. The linker length between CD3epsilon and CD3gamma is critical since scCD3epsilongamma16 containing a 16 residue connector failed to generate a stable heterodimer. Collectively, the results demonstrate that: (i) soluble heterodimeric fragments of CD3 can be produced; (ii) cotranslation of CD3 chains insures proper **folding** even in the absence of the conserved ectodomain stalk region (CxxCxE); and (iii) CD3epsilon has a more stable tertiary protein **fold** than CD3gamma.

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     $0.02  TELNET
     $0.02  Estimated cost this search
     $0.02  Estimated total session cost   0.228 DialUnits

File 340:CLAIMS(R)/US Patent  1950-04/Feb 03
       (c) 2004 IFI/CLAIMS(R)
*File 340: Annual reload and classification updates delayed due
 to processing issues.

      Set  Items  Description
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            4209  ZIPPER
      S1     162  LEUCINE(W)ZIPPER
? s fos
      S2     313  FOS
? s s1 and s2
             162  S1
             313  S2
      S3      22  S1 AND S2
? s c(w)jun
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            5618  JUN
      S4     152  C(W)JUN
? s c(w)fos
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             313  FOS
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      S7       4  S6 AND PY<=1998
? t s7/3,k,ab/1-4

 7/3,K,AB/1
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 2856773  IFI Acc No: 9717689
Document Type: C
USE OF PAIRS OF LEUCINE ZIPPER PEPTIDES IN IMMUNOASSAY METHODS
Inventors: Auerbach Bernhard (DE); Bosslet Klaus (DE); Hermentin Peter (DE)
    ; Muller Rolf (DE); Pfleiderer Peter (DE); Sedlacek Hans Harald (DE)
Assignee: Behringwerke AG DE
Assignee Code: 08592  Document Type: REASSIGNED
Publication (No,Date), Applic (No,Date):
US 5643731    19970701 US 95467943    19950606
Publication Kind:  A
Calculated Expiration: 20140701
(Cited in 002 later patents)  Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19980721
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Continuation Pub(No),Applic(No,Date): ABANDONED US 91805687
19911212; ABANDONED US 9327587 19930305; ABANDONED
US 94182390 19940118; ABANDONED US 94342001
19941116
Priority Applic(No,Date): DE 4040669 19901219

Abstract: The invention relates to a method of using a pair of **leucine zipper** peptides for in vitro diagnosis, in particular, for the immunochemical detection and determination of an analyte in a biological liquid. In one method, the first **leucine zipper** peptide is immobilized by attaching it to a solid support, the second **leucine zipper** peptide is coupled to a specific binding partner for the analyte, the two peptides are brought into contact, the sample of the biological liquid is brought into contact with the immobilized first peptide and the specific binding partner for the analyte, and the amount of analyte bound to the binding partner is determined. The **leucine zipper** peptides are preferably v-**fos** and **c-jun**.

USE OF PAIRS OF **LEUCINE ZIPPER** PEPTIDES IN IMMUNOASSAY METHODS
Publication (No,Date), Applic (No,Date):
...**19970701**

Abstract: The invention relates to a method of using a pair of **leucine zipper** peptides for in vitro diagnosis, in particular, for the immunochemical detection and determination of an analyte in a biological liquid. In one method, the first **leucine zipper** peptide is immobilized by attaching it to a solid support, the second **leucine zipper** peptide is coupled to a specific binding partner for the analyte, the two peptides are...
...the analyte, and the amount of analyte bound to the binding partner is determined. The **leucine zipper** peptides are preferably v-**fos** and **c-jun**.

Exemplary Claim: ...detection and determination of an analyte in a biological liquid using a pair of complementary **leucine zipper** peptides, wherein the first **leucine zipper** peptide of the pair of **leucine zipper** peptides specifically binds to the second **leucine zipper** peptide of the pair of **leucine zipper** peptides, comprising the steps of: (a) immobilizing said first **leucine zipper** peptide on a solid phase; (b) coupling said second **leucine zipper** peptide to a specific binding partner for the analyte; (c) contacting the immobilized first **leucine zipper** peptide with the second **leucine zipper** peptide coupled to the specific binding partner for the analyte, thereby immobilizing the specific binding...
Non-exemplary Claims: ...3. The method of claim 1, wherein the first **leucine zipper** peptide is one of v-**Fos** and **c-Jun** and the second **leucine zipper** peptide is the other
...

...detection and determination of an analyte in a biological liquid using a pair of complementary **leucine zipper** peptides, wherein the first **leucine zipper** peptide of the pair of **leucine zipper** peptides specifically binds to the second **leucine zipper** peptide of the pair **leucine zipper** peptides, comprising the steps of: (a) coupling said first **leucine zipper** peptide to a signal-emitting component; (b) coupling said second **leucine zipper** peptide to a first specific binding partner for the analyte; (c) contacting the first **leucine zipper** peptide coupled to the signal-emimitting component with the second **leucine zipper** peptide coupled to the specific binding partner for the analyte to form a complex; (d...

...6. The method of claim 4, wherein the first **leucine zipper** peptide is one of v-**Fos** and **c-Jun** and the second **leucine zipper** peptide is the other...

...in a biological liquid, consisting essentially of: a solid phase; and a pair of complementary **leucine zipper** peptides consisting of a first **leucine zipper** peptide and a second **leucine zipper** peptide, wherein the first **leucine zipper** peptide of the pair of **leucine zipper** peptides specifically binds to the second **leucine zipper** peptide of the pair of **leucine zipper** peptides; wherein the first **leucine zipper** peptide is immobilized on said solid phase, the second **leucine zipper** peptide is coupled to a specific binding partner for the analyte, and the second **leucine zipper** peptide is complexed with the first **leucine zipper** peptide ...

...determination of an analyte in a biological liquid, consisting essentially of a pair of complementary **leucine zipper** peptides consisting of a first **leucine zipper** peptide and a second **leucine zipper** peptide, wherein the first **leucine zipper** peptide of the pair of **leucine zipper** peptides specifically binds to the second **leucine zipper** peptide of the pair of **leucine zipper** peptides, wherein the first **leucine zipper** peptide is coupled to signal-emitting component and the second **leucine zipper** peptide is coupled to a specific binding partner for the analyte...

...being bound to the specific binding partner, wherein the improvement comprises: (a) immobilizing a first **leucine zipper** peptide of a pair of complementary **leucine zipper** peptides to a solid phase, wherein the first **leucine zipper** peptide of the pair of **leucine zipper** peptides specifically binds to a second **leucine zipper** peptide of the pair of **leucine zipper** peptides; (b) coupling said second **leucine zipper** peptide to a specific binding partner for the analyte; and (c) contacting the first **leucine zipper** peptide with the second **leucine zipper** peptide to immobilize said specific binding Gartner for the analyte to the solid phase...second specific binding partner for the analyte, wherein the improvement comprises: (a) coupling a first **leucine zipper** peptide of a pair of complementary **leucine zipper** peptides to a signal-emitting component, wherein the first **leucine zipper** peptide of the pair of **leucine zipper** peptides specifically binds to a second **leucine zipper** peptide of the pair of **leucine zipper** peptides; (b) coupling said second **leucine zipper** peptide to the second specific binding partner for the analyte; and (c) contacting the first **leucine zipper** peptide with the second **leucine zipper** peptide, thereby attaching the signal-emitting component to the second specific binding partner for the...

...the signal in an immunoassay for an analyte, comprising the steps of: (a) coupling first **leucine zipper** peptides of a pair of **leucine zipper** peptides to a signal-emitting component, wherein the first **leucine zipper** peptides of the pair of **leucine zipper** peptides specifically binds to a second **leucine zipper** peptides; (b) coupling more than one molecule of the second **leucine zipper** peptide to a second specific binding partner which specifically binds to a first specific binding partner which specifically binds to the analyte; (c) contacting the first **leucine zipper** peptides coupled to the signal-emitting components with the second **leucine zipper** peptides coupled to the specific binding partner to form a complex; (d) contacting a sample...

...13. The method of claim 11, wherein the first **leucine zipper** peptide is one of v-**Fos** and **c-Jun** and the second **leucine zipper** peptide is the other...
...second specific binding partner is coupled to the more than one molecules of the second **leucine zipper** peptide via a carrier molecule.

7/3,K,AB/2
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2852080 IFI Acc No: 9716260
Document Type: C
FUNCTIONAL ANTAGONISM BETWEEN PROTO-ONCOPROTEIN **C-JUN** AND HORMONE RECEPTORS; METHOD FOR SELECTING A COMPOUND WHICH DISRUPTS FUNCTION OF ACTIVATOR PROTEIN 1 BUT DOES NOT PROMOTE TRANSCRIPTIONAL ACTIVATION OF STEROID HORMONE RESPONSIVE GENE; FOR SELECTING COMPOUNDS FOR TREATING CELLS UNDERGOING UNCONTROLLED GROWTH
Inventors: Evans Ronald M (US); Schule Ronald (DE)
Assignee: Salk Institute for Biological Studies
Assignee Code: 73756
Publication (No,Date), Applic (No,Date):
US 5639592 **19970617** US 9430330 19940503
Publication Kind: A
Calculated Expiration: 20140617
(Cited in 004 later patents)
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED US 90586187 19900921
PCT Pub(No,Date),Applic(No,Date): WO 925447 **19920402** WO 91US6848 19910920
Section 371: 19940503
Section 102(e):19940503
Priority Applic(No,Date): US 9430330 19940503; US 90586187 19900921

Abstract: Hormone receptors and the transcription factor Jun/AP-1 have been shown to reciprocally repress one another by a mechanism which is independent of DNA binding. For example, over-expression of AP-1 represses glucocorticoid-induced activation of genes carrying a functional glucocorticoid response element. Conversely, glucocorticoid has been shown to repress the transcriptional activation of genes which are controlled by promoters which contain the AP-1 binding site. In addition, methods are disclosed for selecting compounds useful for treating cells undergoing uncontrolled proliferation, such compounds being capable of disrupting the function of AP-1, but display substantially no ability to promote the transcriptional activation of hormone responsive genes.

FUNCTIONAL ANTAGONISM BETWEEN PROTO-ONCOPROTEIN **C-JUN** AND HORMONE RECEPTORS...
Publication (No,Date), Applic (No,Date):
...**19970617**
...PCT Pub(No,Date),Applic(No,Date): **19920402**
Non-exemplary Claims: ...steroid hormone-responsive gene, said method comprising: administering to said system a peptide comprising the **leucine zipper** region of **c-Jun** in an amount ...
11. The method according to claim 10 wherein the molar ratio of the **leucine zipper** region of **c-Jun** to steroid hormone receptor falls in the range of about 0.5:1 up to...

...according to claim 12 wherein said AP-1-responsive gene is a collagenase gene, a **c-Jun** gene, a c-**Fos** gene, an immune-response gene, or a retinoic acid receptor-alpha gene...

7/3,K,AB/3
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2791522 IFI Acc No: 9631248
Document Type: C
BIFUNCTIONAL ANTIBODIES AND METHOD OF PREPARING SAME; FIRST FAB FRAGMENT AND SECOND FAB FRAGMENT STABLY ASSOCIATED THROUGH COMPLEMENTARY DOMAINS WHICH BIND TO FORM **LEUCINE ZIPPER**, FORMING ANTIBODY CONSTRUCT CAPABLE OF BINDING TO TWO ANTIGENIC SITES
Inventors: Curtis Peter J (US)
Assignee: Wistar Institute of Anatomy and Biology The
Assignee Code: 92890
Publication (No,Date), Applic (No,Date):
US 5582996 **19961210** US 94250656 19940527
Publication Kind: A
Calculated Expiration: 20131210
(Cited in 002 later patents) Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19970610
Continuation Pub(No),Applic(No,Date): ABANDONED US 92917074 19920731
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED US 90622983 19901204
Priority Applic(No,Date): US 94250656 19940527; US 92917074 19920731; US 90622983 19901204

Abstract: A recombinant antibody capable of binding to two different antigenic sites, contains Fab fragments from the same or, preferably, different antibodies, which are brought into association by complementary interactive domains which have been inserted into a region of the antibody heavy chain constant region.

...FAB FRAGMENT AND SECOND FAB FRAGMENT STABLY ASSOCIATED THROUGH COMPLEMENTARY DOMAINS WHICH BIND TO FORM **LEUCINE ZIPPER**, FORMING ANTIBODY CONSTRUCT CAPABLE OF BINDING TO TWO ANTIGENIC SITES
Publication (No,Date), Applic (No,Date):
...**19961210**

Exemplary Claim: ...but not to itself, wherein the first and second complementary domains bind to form a **leucine zipper** and to stably associate said first Fab fragment and said second Fab fragment into a...
Non-exemplary Claims: ...but not to itself, whereby the first and second complementary domains interact to form a **leucine zipper** to associate the first and second modified Fab regions into a single antibody construct capable...

...the first complementary domain, wherein the first and second complementary domains bind to form a **leucine zipper** and to stably associate said first Fab fragment and said second Fab fragment into a...

...antibody construct capable of binding to two antigenic sites, wherein said first domain is the **leucine zipper** region of c-**fos** oncogene and said second domain is the **leucine zipper** region of **c-jun** oncogene...

...but not to itself, whereby the first and second complementary domains interact to form a **leucine zipper** to associate the first and second modified Fab regions into a single antibody construct capable of binding to two antigenic sites, wherein the complementary domains are

selected from the **leucine zipper** regions of the oncogenes c-**fos** and **c-jun**.

7/3,K,AB/4
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2666744 IFI Acc No: 9529139
Document Type: C
TRANSDOMINANT NEGATIVE PROTO-ONCOGENE; GENETIC ENGINEERING
Inventors: Verma Inder M (US); Wisdom Ronald M (US); Yen Jong-Young J (US)
Assignee: Salk Institute for Biological Studies
Assignee Code: 73756
Publication (No,Date), Applic (No,Date):
US 5470736 **19951128** US 94218686 19940328
Publication Kind: A
Calculated Expiration: 20121128
(Cited in 005 later patents)
Continuation Pub(No),Applic(No,Date): ABANDONED US 91710862 19910610
Priority Applic(No,Date): US 94218686 19940328; US 91710862 19910610

Abstract: The present invention provides polynucleotide and polypeptide sequences for a trans-repressing protein of the **Fos** protooncogene family, where the polypeptide is characterized by having a **leucine zipper** domain and forming a heterodimer with a Jun related protein. This heterodimer is capable of biding to an AP-1 site and suppressing transcriptional transactivation of a promoter containing the AP-1 site.

Publication (No,Date), Applic (No,Date):
...**19951128**

Abstract: The present invention provides polynucleotide and polypeptide sequences for a trans-repressing protein of the **Fos** protooncogene family, where the polypeptide is characterized by having a **leucine zipper** domain and forming a heterodimer with a Jun related protein. This heterodimer is capable of...

Exemplary Claim: ...encoding a trans-repressing FosB2 protein, wherein the protein is characterized by: (a) having a **leucine zipper** domain; and (b) forming a heterodimer with a Jun related protein, wherein the heterodimer is...
Non-exemplary Claims: ...of claim 1, wherein the Jun related protein is selected from the group consisting of **c-Jun**, Jun B and Jun D
...
?

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2004/Feb W1
         (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
  File  55:Biosis Previews(R)  1993-2004/Jan W4
         (c) 2004 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci  1990-2004/Jan W4
         (c) 2004 Inst for Sci Info
*File  34: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES 34.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
         (c) 1998 Inst for Sci Info
*File 434: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES434.
  File 340:CLAIMS(R)/US Patent  1950-04/Feb 03
         (c) 2004 IFI/CLAIMS(R)
*File 340: Annual reload and classification updates delayed due
 to processing issues.

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u!
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          625054  COLI
      S1  579144  ESCHERICHIA(W)COLI
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Processing
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          778319  YIELD??
      S6   63965  HIGH(5N)YIELD??
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           63965  S6
      S7      28  S5 AND S6
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>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
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Processing
              14  S8
        33644571  PY<=1998
      S9       7  S8 AND PY<=1998
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9/3,K,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10373856 96178941 PMID: 8606152
The regulatory characteristics of yeast fructose-1,6-bisphosphatase confer only a small selective **advantage**.
Navas M A; Gancedo J M
Instituto de Investigaciones Biomedicas, Consejo Superior de Investigaciones Cientificas, Madrid, Spain.
Journal of bacteriology (UNITED STATES) Apr **1996**, 178 (7) p1809-12, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The question of how the loss of regulatory mechanisms for a metabolic enzyme would affect the fitness of the corresponding organism has been addressed. For this, the fructose-1,6-bisphosphatase (FbPase) from Saccharomyces cerevisiae has been taken as a model. Yeast strains in which different controls on FbPase (catabolite repression and inactivation; inhibition by fructose-2,6-bisphosphate and AMP) have been removed have been constructed. These strains **express** during growth on glucose either the native yeast FbPase, the **Escherichia coli** FbPase which is insensitive to inhibition by fructose-2,6-bisphosphate, or a mutated E. coli FbPase with low sensitivity to AMP. **Expression** of the heterologous FbPases increases the fermentation rate of the yeast and its generation time, while it decreases its growth **yield**. In the strain containing **high** levels of an unregulated bacterial FbPase, cycling between fructose-6-phosphate and fructose-1,6-bisphosphate reaches 14%. It is shown that the regulatory mechanisms of FbPase provide a slight but definite competitive **advantage** during growth in mixed cultures.

The regulatory characteristics of yeast fructose-1,6-bisphosphatase confer only a small selective **advantage**.
Apr **1996**,
... by fructose-2,6-bisphosphate and AMP) have been removed have been constructed. These strains **express** during growth on glucose either the native yeast FbPase, the **Escherichia coli** FbPase which is insensitive to inhibition by fructose-2,6-bisphosphate, or a mutated E. coli FbPase with low sensitivity to AMP. **Expression** of the heterologous FbPases increases the fermentation rate of the yeast and its generation time, while it decreases its growth **yield**. In the strain containing **high** levels of an unregulated bacterial FbPase, cycling between fructose-6-phosphate and fructose-1,6...

... It is shown that the regulatory mechanisms of FbPase provide a slight but definite competitive **advantage** during growth in mixed cultures.
; Adenosine Monophosphate--metabolism--ME; **Escherichia coli** --enzymology--EN; Fructose-Bisphosphatase--genetics--GE; Gene **Expression** Regulation, Fungal; Glucose--metabolism--ME; Recombinant Proteins --genetics--GE; Recombinant Proteins--metabolism--ME; Saccharomyces cerevisiae...

9/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10344444 96146908 PMID: 8588916
Single-step purification of a thermostable DNA polymerase **expressed** in **Escherichia coli**.

Desai U J; Pfaffle P K
Department of Life Sciences, Indiana State University, Terre Haute 47809, USA.
BioTechniques (UNITED STATES) Nov **1995**, 19 (5) p780-2, 784, ISSN 0736-6205 Journal Code: 8306785
Document type: Technical Report
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The coding region of the gene for Taq DNA polymerase has been cloned into the common vector pUC18. Using a single-step procedure, large amounts of active enzyme can be purified from **Escherichia coli** carrying this construct. This procedure takes **advantage** of the thermostable properties of the DNA polymerase. This simple procedure gives very **high yields** of essentially homogeneous, highly active enzyme suitable for use in molecular biological applications. Yields are over two orders of magnitude greater than available with current methods.
Single-step purification of a thermostable DNA polymerase **expressed** in **Escherichia coli**.
Nov **1995**,
... pUC18. Using a single-step procedure, large amounts of active enzyme can be purified from **Escherichia coli** carrying this construct. This procedure takes **advantage** of the thermostable properties of the DNA polymerase. This simple procedure gives very **high yields** of essentially homogeneous, highly active enzyme suitable for use in molecular biological applications. Yields are...
Descriptors: DNA-Directed DNA Polymerase--isolation and purification--IP; ***Escherichia coli**--genetics--GE; Base Sequence; Cloning, Molecular; DNA-Directed DNA Polymerase--genetics--GE; Electrophoresis, Polyacrylamide Gel; Enzyme Stability; **Escherichia coli** --enzymology--EN; Gene **Expression**; Genetic Vectors; Heat; Molecular Sequence Data; Polymerase Chain Reaction; Taq Polymerase

9/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08191784 94257706 PMID: 8199219
Purification of recombinant adenomatous polyposis coli polypeptide chains from E. coli extracts by continuous-elution electrophoresis.
Kraus C; Klein E; Ballhausen W G
Institut fuer Humangenetik, Universitaet Erlangen-Nuernberg, Germany.
Applied and theoretical electrophoresis - the official journal of the International Electrophoresis Society (ENGLAND) **1993**, 3 (6) p271-5, ISSN 0954-6642 Journal Code: 8915308
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A polypeptide chain encoded by the exons 1-3 of the human adenomatous polyposis coli (APC) tumor suppressor gene was **expressed** as a maltose binding fusion protein (MBP) in E. coli to be used for immunization purposes. It turned out, that the APC-MBP fusion product of 60 kDa was deposited in bacterial inclusion bodies and, in addition, it was not retarded by an amylose affinity column, most probably due to an altered conformation of the chimeric molecule. For this reason, we established an alternative purification scheme, which took **advantage** of SDS-extraction followed by a high-resolution two-step continuous-elution electrophoresis (CEE) procedure. This purification method allowed us to obtain **high yields** of pure human APC exon 1-3-encoded proteins.
The final yield of the pure APC polypeptide chains was estimated to represent 5-8% of the amount of SDS-extracted E. coli lysate subjected to the first cycle of CEE. The purified APC molecules were successfully used

for the development of specific antibodies. The CEE procedure described here represents a general purification method which is valuable in cases where fusion proteins are deposited as inclusion bodies in bacteria, or if affinity chromatography is precluded due to a conformation-induced lack of ligand binding of the chimeric molecule.

1993,
... the exons 1-3 of the human adenomatous polyposis coli (APC) tumor suppressor gene was **expressed** as a maltose binding fusion protein (MBP) in E. coli to be used for immunization...

...of the chimeric molecule. For this reason, we established an alternative purification scheme, which took **advantage** of SDS-extraction followed by a high-resolution two-step continuous-elution electrophoresis (CEE) procedure. This purification method allowed us to obtain **high yields** of pure human APC exon 1-3-encoded proteins. The final yield of the pure...
; Base Sequence; Cloning, Molecular; Electrophoresis--methods--MT; **Escherichia coli**; Molecular Sequence Data; Neoplasm Proteins --biosynthesis--BI; Neoplasm Proteins--genetics--GE; Peptide Synthesis; Peptides--genetics...

9/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07281382 92144101 PMID: 1368756
Utilization of trans-activated T4 uvsY regulatory signal for a **high yield** of cloned gene products.
Noguchi T; Takahashi H
Research Laboratories, Yamasa Shoyu Co., Ltd., Chiba, Japan.
Agricultural and biological chemistry (JAPAN) Oct **1991**, 55 (10) p2497-506, ISSN 0002-1369 Journal Code: 0370452
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We established an efficient system for a high-level production of foreign gene products in **Escherichia coli** using a trans-activated gene **expression** under the control of a phage T4 regulatory signal cloned in a plasmid by T4 phage infection. The transcriptional and translational signal of the T4 uvsY gene cloned in a plasmid was fused translationally with the coding region of the lacZ gene. When E. coli cells carrying the uvsY-lacZ plasmid were infected with cytosine-substituting T4 phage at a multiplicity of infection of 5, the amount of beta-galactosidase increased about 2-fold (trans-activation) over that without phage infection. We examined conditions for the high-level production of a trans-activated gene product. We found that a large number of T4-infected cells in a lysis-inhibition state could be obtained by a low multiplicity of infection with cytosine-substituting T4 phage. Thus it is now possible to attain a **high yield** of the trans-activated gene products. We discuss the **advantage** of the trans-activated T4 uvsY regulatory signal for production of foreign products.

Utilization of trans-activated T4 uvsY regulatory signal for a **high yield** of cloned gene products.
Oct **1991**,
We established an efficient system for a high-level production of foreign gene products in **Escherichia coli** using a trans-activated gene **expression** under the control of a phage T4 regulatory signal cloned in a plasmid by T4...

... of infection with cytosine-substituting T4 phage. Thus it is now

possible to attain a **high yield** of the trans-activated gene products. We discuss the **advantage** of the trans-activated T4 uvsY regulatory signal for production of foreign products.
Descriptors: Bacterial Proteins--genetics--GE; *Gene **Expression** Regulation, Bacterial--genetics--GE; *Regulatory Sequences, Nucleic Acid --genetics--GE; *T-Phages--genetics--GE; *Trans...
; Amino Acid Sequence; Base Sequence; Cloning, Molecular; Cytosine --physiology--PH; DNA, Recombinant--genetics--GE; **Escherichia coli**--genetics--GE; Molecular Sequence Data; Promoter Regions (Genetics)--genetics--GE

9/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07026078 91266933 PMID: 2050135
Single-step purification and structural characterization of human interleukin-6 produced in **Escherichia coli** from a T7 RNA polymerase **expression** vector.
Arcone R; Pucci P; Zappacosta F; Fontaine V; Malorni A; Marino G; Ciliberto G
Dipartimento di Biochimica e Biotecnologie Mediche, II Facolta di Medicina e Chirurgia, Universita di Napoli, Italy.
European journal of biochemistry / FEBS (GERMANY) Jun 15 **1991**, 198 (3) p541-7, ISSN 0014-2956 Journal Code: 0107600
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Human interleukin-6 or B-cell stimulatory factor-2 is a cytokine involved in acute phase and immune response. Cloning of cDNA for human interleukin-6 in the pT7.7 **expression** plasmid under the control of a bacteriophage T7 RNA polymerase promoter system allows rapid production of the cytokine in **Escherichia coli** . Upon cell induction with isopropyl thiogalactopyranoside, recombinant human interleukin-6 is overexpressed and forms insoluble inclusion bodies. Solubilization of the protein with 6 M guanidine hydrochloride and refolding in the presence of a reduction/oxidation system results in a quantitative recovery of recombinant human interleukin-6. This material is already 70% pure and can be further purified to homogeneity with a single passage over a weak anionic-exchange column. Extended structural characterization of the purified protein by electrospray mass spectrometry, automated Edman degradation and peptide mapping by high-pressure liquid chromatography/fast-atom-bombardment mass spectrometry demonstrates that recombinant human interleukin-6 is identical to the natural protein both in amino acid sequence and S-S bridge content. However, it contains a minor component accounting for about 20% of the entire translated protein which exhibits a Met-Ala dipeptide extension at the N-terminus. Purified recombinant human interleukin-6 is biologically active because it is able to induce at least 70-fold the human C-reactive promoter transfected in human hepatoma Hep 3B cells and is stable for several months in 10% glycerol at 4 degrees C. The **expression** system described in the present work has the main **advantage** of producing a **high yield** of recombinant human interleukin-6 (about 25 mg/l) combined with a very simple purification scheme.

Single-step purification and structural characterization of human interleukin-6 produced in **Escherichia coli** from a T7 RNA polymerase **expression** vector.
Jun 15 **1991**,
... phase and immune response. Cloning of cDNA for human interleukin-6 in the pT7.7 **expression** plasmid under the control of a bacteriophage T7 RNA polymerase promoter system allows rapid production of the cytokine in

Escherichia coli . Upon cell induction with isopropyl thiogalactopyranoside, recombinant human interleukin-6 is overexpressed and forms insoluble...

... cells and is stable for several months in 10% glycerol at 4 degrees C. The **expression** system described in the present work has the main **advantage** of producing a **high yield** of recombinant human interleukin-6 (about 25 mg/l) combined with a very simple purification...
Descriptors: DNA-Directed RNA Polymerases--genetics--GE; * **Escherichia coli**--genetics--GE; *Interleukin-6--isolation and purification--IP; *T-Phages--genetics--GE

9/3,K,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06853210 91093287 PMID: 1985969
Cloning, sequencing, and overexpression of genes for ribosomal proteins from Bacillus stearothermophilus.
Ramakrishnan V; Gerchman S E
Biology Department, Brookhaven National Laboratory, Upton, New York 11973.
Journal of biological chemistry (UNITED STATES) Jan 15 **1991**, 266 (2) p880-5, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Although a low resolution model for the arrangement of the proteins of the small and large ribosomal subunits is known, a detailed mechanistic understanding of the function of the ribosome awaits a high resolution structure of its components. While crystals have been obtained of several ribosomal proteins from Bacillus stearothermophilus, determination of atomic resolution structures of these proteins is impeded by the difficulty of obtaining large amounts of native proteins for crystallographic or NMR studies. We describe here the cloning and overexpression in **Escherichia coli** of the genes for ribosomal proteins S5, L6, L9, and L18 from B. stearothermophilus. S5 is extremely toxic to E. coli when overexpressed, and we have taken **advantage** of a new tightly regulated **expression** system to obtain **high yields** (more than 100 mg of pure protein/liter of culture) of this protein. The B. stearothermophilus S5 produced in E. coli crystallizes, and the crystals are identical to those obtained from the native protein. The crystals diffract to 2-A resolution.

Jan 15 **1991**,
... native proteins for crystallographic or NMR studies. We describe here the cloning and overexpression in **Escherichia coli** of the genes for ribosomal proteins S5, L6, L9, and L18 from B. stearothermophilus. S5 is extremely toxic to E. coli when overexpressed, and we have taken **advantage** of a new tightly regulated **expression** system to obtain **high yields** (more than 100 mg of pure protein/liter of culture) of this protein. The B...
Descriptors: Bacillus stearothermophilus--metabolism--ME; *Gene **Expression** Regulation, Bacterial; *Genes, Bacterial; *Ribosomal Proteins--genetics--GE...; Bacillus stearothermophilus--genetics--GE; Base Sequence; Cloning, Molecular; DNA, Bacterial--genetics--GE; Electrophoresis, Polyacrylamide Gel; **Escherichia coli**--genetics --GE; Molecular Sequence Data; Polymerase Chain Reaction

9/3,K,AB/7 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04505586 Genuine Article#: TH829 Number of References: 27
Title: SECRETION OF BIOLOGICALLY-ACTIVE HUMAN PROAPOLIPOPROTEIN A-I IN A BACULOVIRUS-INSECT CELL SYSTEM - PROTECTION FROM DEGRADATION BY PROTEASE INHIBITORS (Abstract Available)
Author(s): PYLE LE; BARTON P; FUJIWARA Y; MITCHELL A; FIDGE N
Corporate Source: BAKER MED RES INST,LIPOPROT & ATHEROSCLEROSIS UNIT/PRAHRAN/VIC 3181/AUSTRALIA/; BAKER MED RES INST,LIPOPROT & ATHEROSCLEROSIS UNIT/PRAHRAN/VIC 3181/AUSTRALIA/; SWINBURNE UNIV TECHNOL/HAWTHORN/VIC 3122/AUSTRALIA/
Journal: JOURNAL OF LIPID RESEARCH, **1995**, V36, N11 (NOV), P2355-2361
ISSN: 0022-2275
Language: ENGLISH Document Type: ARTICLE
Abstract: Studies of the structure and function of apolipoprotein A-I (apoA-I) often require its purification by delipidation of high density lipoprotein isolated from large quantities of human plasma and separation of apoA-I from other plasma apolipoproteins. To reduce the need for extensive purification procedures, we have developed an insect cell/baculovirus **expression** system for the production and secretion of human proapoA-I. The recombinant baculovirus containing full-length human apoA-I cDNA, when introduced into Spodoptera frugiperda, directs the synthesis of preproapoA-I, which is subsequently secreted into the growth medium as proapoA-I, indicating correct processing of the signal peptide during secretion. To prevent the extensive degradation of secreted proapoA-I, leupeptin and pepstatin A were added to the serum free cell culture medium. The protein was simply purified by filtration of the medium, which contained up to 80 mg/l proapoA-I, followed by chromatography on phenyl-sepharose CL-4B. The resultant proapoA-I was found to bind lipid and to activate lecithin:cholesterol acyltransferase as effectively as apoA-I from human plasma. The **advantage** of this **expression** system is the ease of purification of intact, biologically active apoA-I in **high yield**.

, **1995**
...Abstract: To reduce the need for extensive purification procedures, we have developed an insect cell/baculovirus **expression** system for the production and secretion of human proapoA-I. The recombinant baculovirus containing full...

...and to activate lecithin:cholesterol acyltransferase as effectively as apoA-I from human plasma. The **advantage** of this **expression** system is the ease of purification of intact, biologically active apoA-I in **high yield**.
...Identifiers--LECITHIN-CHOLESTEROL ACYLTRANSFERASE; VIRUS **EXPRESSION** VECTORS; HIGH-DENSITY-LIPOPROTEIN; HUMAN APOLIPOPROTEIN-E; **ESCHERICHIA-COLI**; BINDING DOMAIN; CONVERSION; ANTIBODIES; PARTICLES; RECEPTOR
...Research Fronts: LIPOPROTEIN RECEPTOR; LDL METABOLISM; HEPG2 CELLS; CHOLESTEROL-FED RABBITS; TRANSGENIC MICE)
93-2767 001 (BACULOVIRUS **EXPRESSION** SYSTEM; INSECT CELLS; AUTOGRAPHA-CALIFORNICA NUCLEAR POLYHEDROSIS-VIRUS; RECOMBINANT VIRAL INSECTICIDES)
93-3796 001 (HIGH...
?

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2004/Jan W3
         (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
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*File  34: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES 34.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
         (c) 1998 Inst for Sci Info
*File 434: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES434.
  File 340:CLAIMS(R)/US Patent  1950-03/Jan 20
         (c) 2004 IFI/CLAIMS(R)
*File 340: Enter HELP NEWS340 & HELP ALERTS340 for search,
 display & Alert information.

      Set  Items  Description
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? s TCR or T(2n)receptor
           45365  TCR
         4710039  T
         1632467  RECEPTOR
           94552  T(2N)RECEPTOR
      S1  112057  TCR OR T(2N)RECEPTOR
? s disulfide
      S2   75854  DISULFIDE
? s s1 and s2
          112057  S1
           75854  S2
      S3    1810  S1 AND S2
? s detrimental
      S4   37324  DETRIMENTAL
? s s3 and s4
            1810  S3
           37324  S4
      S5       0  S3 AND S4
? s fold?
      S6  714834  FOLD?
? s s3 and s6
            1810  S3
          714834  S6
      S7     129  S3 AND S6
? s unstabl? or aggregat?
          119811  UNSTABL?
          315431  AGGREGAT?
      S8  431131  UNSTABL? OR AGGREGAT?
? s s7 and s8
             129  S7
          431131  S8
      S9      18  S7 AND S8
? rd
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...completed examining records
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? t s10/3,k,ab/1-15

 10/3,K,AB/1     (Item 1 from file: 155)
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DIALOG(R)File 155:MEDLINE(R)

11705318 99141420 PMID: 9917415

Folding, heterodimeric association and specific peptide recognition of a murine alphabeta **T**-cell **receptor** expressed in Escherichia coli.

Pecorari F; Tissot A C; Pluckthun A

Biochemisches Institut, Universitat Zurich, Winterthurerstr. 190, Zurich, CH-8057, Switzerland.

Journal of molecular biology (ENGLAND) Jan 29 1999, 285 (4) p1831-43 , ISSN 0022-2836 Journal Code: 2985088R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

In a systematic study of the murine **T**-cell **receptor** UZ3-4, expressed and refolded from inclusion bodies in Escherichia coli, it was found that functional molecules can be obtained only under a very narrow set of conditions. The refolded **T**-cell **receptor** UZ3-4 specifically recognizes its cognate peptide (from mycobacterial Hsp60) in the context of H-2Db, but not another peptide bound to H-2Db, and the dissociation constant was determined by BIAcore as 10(-4) M. Using **T**-cell **receptor** constructs comprising all extracellular domains (ValphaCalpha and VbetaCbeta), found to be necessary for stability of the final product, significant amounts of native molecules were obtained only if the intermolecular Calpha-Cbeta **disulfide** bridge bond was deleted, even though the interaction between the complete alpha and beta-chain was determined to be very weak and fully reversible (KD approximately 10(-7) to 10(-6) M). Fusion of Jun and Fos to the constant domains also decreased the **folding** yield, because of premature association of intermediates leading to **aggregation**. Furthermore, only in a very narrow set of concentrations of oxidized and reduced glutathione, native **disulfide** bonds dominated. This shows that **T**-cell **receptor** domains are very prone to **aggregation** and misassociation during **folding**, compounded by incorrect **disulfide** bond formation. Once **folded**, however, the heterodimeric molecule is very stable and could be concentrated to millimolar concentration. Copyright 1999 Academic Press.

Folding, heterodimeric association and specific peptide recognition of a murine alphabeta **T**-cell **receptor** expressed in Escherichia coli.

In a systematic study of the murine **T**-cell **receptor** UZ3-4, expressed and refolded from inclusion bodies in Escherichia coli, it was found that functional molecules can be obtained only under a very narrow set of conditions. The refolded **T**-cell **receptor** UZ3-4 specifically recognizes its cognate peptide (from mycobacterial Hsp60) in the context of H...

...H-2Db, and the dissociation constant was determined by BIAcore as 10(-4) M. Using **T**-cell **receptor** constructs comprising all extracellular domains (ValphaCalpha and VbetaCbeta), found to be necessary for stability of...

... final product, significant amounts of native molecules were obtained only if the intermolecular Calpha-Cbeta **disulfide** bridge bond was deleted, even though the interaction between the complete alpha and beta-chain...

... 10(-6) M). Fusion of Jun and Fos to the constant domains also decreased the **folding** yield, because of premature association of intermediates leading to **aggregation**. Furthermore, only in a very narrow set of concentrations of oxidized and reduced glutathione, native **disulfide** bonds dominated. This shows that **T**-cell **receptor** domains are

very prone to **aggregation** and misassociation during **folding**, compounded by incorrect **disulfide** bond formation. Once **folded**, however, the heterodimeric molecule is very stable and could be concentrated to millimolar concentration. Copyright...
...; CH; Ligands; Mice; Molecular Sequence Data; Peptides--chemistry--CH; Peptides--metabolism--ME; Protein Conformation; Protein **Folding**; Receptors, Antigen, T-Cell, alpha-beta--genetics--GE; Recombinant Proteins --chemistry--CH; Recombinant Proteins--genetics...

10/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11106161 97400339 PMID: 9257833
Recombinant soluble alphabeta T cell receptors protect T cells from immune suppression: requirement for **aggregated** multimeric, **disulfide**-linked alphabeta heterodimers.
Paliwal V; Ptak W; Sperl J; Braswell E; Askenase P W
Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520, USA.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Aug 15 1997, 159 (4) p1718-27, ISSN 0022-1767 Journal Code: 2985117R
Contract/Grant No.: AI-12211; AI; NIAID; AI-26689; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Recombinant soluble T cell receptors (sTCR) protected contact sensitivity (CS) effector T cells from down-regulation or immunosuppression. CS-protecting sTCR were released enzymatically from the surface of thymoma cells transfected with cDNAs encoding **TCR** -alpha and -beta extracellular domains that were expressed with a phosphatidylinositol linkage. sTCR affinity purified on anti-**TCR**-alpha and anti-**TCR** -beta mAb columns had identical CS-protective activity, as did sTCR from a CD4+ Th2 clone or from a CD8+ cytotoxic clone. Reduced sTCR alpha- and beta-chains had no CS-protective activity, but this was restored when the **TCR** chains were rejoined into **disulfide** -linked alphabeta heterodimers. sTCR CS protection was Ag nonspecific, MHC unrestricted, and not influenced by the relevant synthetic peptide specific for the **TCR** complexed with appropriate MHC. CS protection may have resided in the sTCR constant region. When heated at 62 degrees C for 30 min, sTCR formed a CS-protecting **aggregate** , with a molecular mass of 481 +/- 37 kDa, corresponding to an alphabeta **TCR** pentamer. HPLC gel filtration essentially confirmed the molecular mass at 516 kDa for the multimer, while the monomer, which was an alphabeta **TCR** heterodimer, had an expected molecular mass of approximately 104 kDa and no bioactivity. In summary, the pentameric sTCR may bind to and activate lymphoid cells, perhaps via constant domains, resulting in protection of CS effector T cells from down-regulation. The ability of sTCR to protect CS effector T cells from down-regulation/suppression, if generalized, could overcome immunosuppression accompanying infectious diseases, particularly AIDS, or in tumors.

Recombinant soluble alphabeta T cell receptors protect T cells from immune suppression: requirement for **aggregated** multimeric, **disulfide**-linked alphabeta heterodimers.
... protecting sTCR were released enzymatically from the surface of thymoma cells transfected with cDNAs encoding **TCR**-alpha and -beta extracellular domains that were expressed with a phosphatidylinositol linkage. sTCR affinity purified on anti-**TCR**-alpha and anti-**TCR** -beta mAb columns had identical CS-protective activity, as did sTCR from a CD4+ Th2...

... alpha- and beta-chains had no CS-protective activity, but this was restored when the **TCR** chains were rejoined into **disulfide** -linked alphabeta heterodimers. sTCR CS protection was Ag nonspecific, MHC unrestricted, and not influenced by the relevant synthetic peptide specific for the **TCR** complexed with appropriate MHC. CS protection may have resided in the sTCR constant region. When heated at 62 degrees C for 30 min, sTCR formed a CS-protecting **aggregate**, with a molecular mass of 481 +/- 37 kDa, corresponding to an alphabeta **TCR** pentamer. HPLC gel filtration essentially confirmed the molecular mass at 516 kDa for the multimer, while the monomer, which was an alphabeta **TCR** heterodimer, had an expected molecular mass of approximately 104 kDa and no bioactivity. In summary...
...; prevention and control--PC; Disulfides--chemistry--CH; Electrophoresis, Polyacrylamide Gel; Mice; Mice, Inbred CBA; Protein **Folding**; Recombinant Proteins--pharmacology--PD

10/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06183234 89198838 PMID: 2522980
Production and characterization of monoclonal antibodies to Fc gamma 2a-binding protein isolated from the detergent lysate of a murine macrophagelike cell line, P388D1.
Kagami M; Funatsu Y; Suzuki T
Department of Microbiology, Molecular Genetics, and Immunology, University of Kansas Medical Center, Kansas City 66103.
Journal of leukocyte biology (UNITED STATES) Apr 1989, 45 (4) p311-21, ISSN 0741-5400 Journal Code: 8405628
Contract/Grant No.: AI22742; AI; NIAID; CA35977; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hybridoma cell lines were produced by fusion of SP2/0 murine myeloma cell line with the spleen cells of Wister rats which were immunized with IgG2a-binding protein isolated from the detergent lysate of a murine macrophagelike cell line, P388D1, by affinity chromatography on IgG-Sepharose 4B. A monoclonal clone (designated as 3A2) out of a total of 13 different antibody-secreting cell lines was found to secrete IgG1 class antibodies, which inhibited more than 70% of the binding of radio-iodinated myeloma IgG2a protein to P388D1 cells. The 3A2 Fab fragments bound specifically to P388D1 cells at 4 degrees C with a KD of 1.9 x 10(-8) M and Bmax of 2.9 x 10(5) per cell. This Fab fragment also specifically bound to Fc gamma 2a **receptor** (R)-positive **T** cell line (S49) with a KD of 4.4 x 10(-9) M and a Bmax of 1.0 x 10(4) but did not bind to Fc gamma 2a-negative S49 variant cell line, cyc-. The flow cytometric analysis with the use of fluorescein-isothiocyanate-tagged 3A2 F(ab')2 also showed that this antibody binds to Fc gamma 2aR-positive cells, P388D1 and S49, but not to Fc gamma 2aR-negative cells, cyc-. Monomeric and heat-**aggregated** IgG2a (13-**fold** molar excess) inhibited the binding of the radioiodinated 3A2 F(ab')2 to P388D1 cells by 70 and 49%, respectively, whereas the inhibition by monomeric and heat-**aggregated** IgG2b was 17 and 39%, respectively; 3A2 F(ab')2 (100-**fold** molar excess) inhibited the binding of IgG2a and IgG2b to P388D1 cells by 90 and 24%, respectively, whereas the inhibition of binding of these IgG to S49 cells was 79 and 49%, respectively. Western blotting analysis showed that 3A2 antibody recognizes a major protein (Mr = 100,000) and a minor component (Mr = 80,000) separated by SDS-PAGE of P388D1 or S49 cell lysates under nonreducing condition, whereas under reducing condition, this antibody recognized a major protein (Mr = 50,000) and two additional minor components (Mr = 40,000 and 35,000). Fc gamma 2aR may thus exist at the cell surface as a **disulfide** linked dimer of a subunit of Mr of 50,000, which could be

partially degraded during the isolation to smaller fragments of 40,000 and 35,000 Mr peptides which are still held together by interchain **disulfide** bond. (ABSTRACT TRUNCATED AT 250 WORDS)

... x 10(5) per cell. This Fab fragment also specifically bound to Fc gamma 2a **receptor** (R)-positive **T** cell line (S49) with a KD of 4.4 x 10(-9) M and a...

... P388D1 and S49, but not to Fc gamma 2aR-negative cells, cyc-. Monomeric and heat-**aggregated** IgG2a (13-**fold** molar excess) inhibited the binding of the radioiodinated 3A2 F(ab')2 to P388D1 cells by 70 and 49%, respectively, whereas the inhibition by monomeric and heat-**aggregated** IgG2b was 17 and 39%, respectively; 3A2 F(ab')2 (100-**fold** molar excess) inhibited the binding of IgG2a and IgG2b to P388D1 cells by 90 and ...

...and 35,000). Fc gamma 2aR may thus exist at the cell surface as a **disulfide** linked dimer of a subunit of Mr of 50,000, which could be partially degraded...

... of 40,000 and 35,000 Mr peptides which are still held together by interchain **disulfide** bond. (ABSTRACT TRUNCATED AT 250 WORDS)

10/3,K,AB/4 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09056476 Genuine Article#: 361QZ Number of References: 131
Title: Protein glucosylation and its role in protein **folding** (ABSTRACT AVAILABLE)
Author(s): Parodi AJ (REPRINT)
Corporate Source: UNIV SAN MARTIN,INST INVEST BIOTECHNOL, CASILLA CORREO 30/RA-1650 SAN MARTIN/BUENOS AIRES/ARGENTINA/ (REPRINT); FDN CAMPOMAR,INST INVEST BIOQUIM/RA-1405 BUENOS AIRES/DF/ARGENTINA/
Journal: ANNUAL REVIEW OF BIOCHEMISTRY, 2000, V69, P69-93
ISSN: 0066-4154 Publication date: 20000000
Publisher: ANNUAL REVIEWS, 4139 EL CAMINO WAY, PO BOX 10139, PALO ALTO, CA 94303-0139
Language: English Document Type: REVIEW
Abstract: An unconventional mechanism for retaining improperly **folded** glycoproteins and facilitating acquisition of their native tertiary and quaternary structures operates in the endoplasmic reticulum. Recognition of **folding** glycoproteins by two resident lectins, membrane-bound calnexin and its soluble homolog, calreticulin, is mediated by protein-linked monoglucosylated oligosaccharides. These oligosaccharides contain glucose (Glc), mannose (Man), and N-acetylglucosamine (GlcNAc) in the general form Glc(1)Man(7-9)GlcNAc(2). They are formed by glucosidase I- and II-catalyzed partial deglucosylation of the oligosaccharide transferred from dolichol diphosphate derivatives to Asn residues in nascent polypeptide chains (Glc(3)Man(9)GlcNAc(2)). Further deglucosylation of the oligosaccharides by glucosidase II liberates glycoproteins from their calnexin/calreticulin anchors. Monoglucosylated glycans are then recreated by the UDP-Glc:glycoprotein glucosyltransferase (GT), and thus recognized again by the lectins, only when linked to improperly **folded** protein moieties, as GT behaves as a sensor of glycoprotein conformations. The deglucosylation-reglucosylation cycle continues until proper **folding** is achieved. The lectin-monoglucosylated oligosaccharide interaction is one of the alternative ways by which cells retain improperly **folded** glycoproteins in the endoplasmic reticulum. Although it decreases the **folding** rate, it, increases **folding** efficiency, prevents premature glycoprotein oligomerization and degradation, and suppresses

formation of nonnative **disulfide** bonds by hindering **aggregation** and thus allowing interaction of protein moieties of **folding** glycoproteins with classical chaperones and other proteins that assist in **folding**.

Title: Protein glucosylation and its role in protein **folding**
Abstract: An unconventional mechanism for retaining improperly **folded** glycoproteins and facilitating acquisition of their native tertiary and quaternary structures operates in the endoplasmic reticulum. Recognition of **folding** glycoproteins by two resident lectins, membrane-bound calnexin and its soluble homolog, calreticulin, is mediated...

...glycoprotein glucosyltransferase (GT), and thus recognized again by the lectins, only when linked to improperly **folded** protein moieties, as GT behaves as a sensor of glycoprotein conformations. The deglucosylation-reglucosylation cycle continues until proper **folding** is achieved. The lectin-monoglucosylated oligosaccharide interaction is one of the alternative ways by which cells retain improperly **folded** glycoproteins in the endoplasmic reticulum. Although it decreases the **folding** rate, it, increases **folding** efficiency, prevents premature glycoprotein oligomerization and degradation, and suppresses formation of nonnative **disulfide** bonds by hindering **aggregation** and thus allowing interaction of protein moieties of **folding** glycoproteins with classical chaperones and other proteins that assist in **folding**.
...Identifiers--N-LINKED OLIGOSACCHARIDES; GLC-GLYCOPROTEIN GLUCOSYLTRANSFERASE; ENDOPLASMIC-RETICULUM MEMBRANE; MOLECULAR CHAPERONES CALNEXIN; VESICULAR STOMATITIS-VIRUS; **TCR** -ALPHA-PROTEINS; HISTOCOMPATIBILITY COMPLEX-MOLECULES; NICOTINIC ACETYLCHOLINE-RECEPTOR; HIGH-MANNOSE OLIGOSACCHARIDES

10/3,K,AB/5 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04007642 Genuine Article#: QY506 Number of References: 35
Title: CROSSRECOGNITION BY CD8 **T**-CELL **RECEPTOR**-ALPHA-BETA CYTOTOXIC T-LYMPHOCYTES OF PEPTIDES IN THE SELF AND THE MYCOBACTERIAL HSP60 WHICH SHARE INTERMEDIATE SEQUENCE HOMOLOGY (Abstract Available)
Author(s): ZUGEL U; SCHOEL B; YAMAMOTO S; HENGEL H; MOREIN B; KAUFMANN SHE
Corporate Source: UNIV ULM,DEPT IMMUNOL/D-89070 ULM//GERMANY/; UNIV ULM,DEPT IMMUNOL/D-89070 ULM//GERMANY/; INST PUBL HLTH,DEPT VET PUBL HLTH/TOKYO 108//JAPAN/; UNIV HEIDELBERG,DEPT VIROL/HEIDELBERG//GERMANY/ ; NATL VET INST,DEPT VIROL/S-75123 UPPSALA//SWEDEN/
Journal: EUROPEAN JOURNAL OF IMMUNOLOGY, 1995, V25, N2 (FEB), P451-458
ISSN: 0014-2980
Language: ENGLISH Document Type: ARTICLE
Abstract: Immunization of C57BL/6 mice with the mycobacterial heat shock protein (hsp) 60 in immunostimulating complexes caused the in vivo activation of autoreactive histocompatibility complex class I (H-2D(b))-restricted CD8 **T** cell **receptor** (**TcR**) alpha/beta cells. A CD8 **TcR** alpha/beta clone with specificity for the mycobacterial hsp60 peptide(499-508) was derived from this immunization,which, in addition, recognized syngeneic macrophages which had been stressed by interferon-gamma (IFN-gamma) stimulation. The stress-induced, self peptide could be extracted from IFN-gamma-stressed macrophages by acid elution, suggesting that the IFN-gamma-induced self peptide is derived from an endogenous protein. Based on our observation that lysis of stressed target cells by this cytotoxic T lymphocyte (CTL) clone was specifically inhibited by hsp60-specific antisense oligonucleotides, we used synthetic peptides representing amino acid (aa) sequences of the murine hsp60 for target cell sensitization and

identification of the relevant self peptide. Synthetic peptides representing 9-mer to 11-mer aa sequences of the murine hsp60 with asparagine in anchor position 4 or 5 as the minimal requirement for H-2D(b) binding were tested in CTL assays. The overlapping murine hsp60 peptides(162-170/171) were stimulatory at a concentration as low as 10-100 pM. Seven other peptides of the murine hsp60 required intermediate peptide concentrations of 10-100 nM for recognition by the CTL clone. Although the murine and mycobacterial hsp60 peptides recognized by this CTL clone showed only intermediate homology (3 identical and 3 similar aa), our data suggest that endogenous hsp60 itself is the source of self peptide(s) presented by IFN-gamma-stressed macrophages to the cross-reactive CTL clone with promiscuous specificity. This notion is consistent with the idea of hsp as a link between infection and autoimmunity.

Title: CROSSRECOGNITION BY CD8 **T**-CELL **RECEPTOR**-ALPHA-BETA CYTOTOXIC T-LYMPHOCYTES OF PEPTIDES IN THE SELF AND THE MYCOBACTERIAL HSP60 WHICH...
...Abstract: the in vivo activation of autoreactive histocompatibility complex class I (H-2D(b))-restricted CD8 **T** cell **receptor** (**TcR**) alpha/beta cells. A CD8 **TcR** alpha/beta clone with specificity for the mycobacterial hsp60 peptide(499-508) was derived from...
...Research Fronts: T-LYMPHOCYTES; ANTIGEN PROCESSING)
93-0448 001 (SOLID-PHASE PEPTIDE-SYNTHESIS; AMINO PROTECTING GROUPS; CYCLIC **DISULFIDE** ANALOGS; FMOC CLEAVAGE)
93-1602 001 (PROTEIN **FOLDING**; MOLECULAR CHAPERONES; **AGGREGATION** OF MAMMALIAN MITOCHONDRIAL MALATE-DEHYDROGENASE INVITRO)
93-4806 001 (INDUCTION OF CD8+ CYTOTOXIC T-LYMPHOCYTES...

...I MHC-RESTRICTED CTL EPITOPES)
93-6931 001 (HEAT-SHOCK PROTEINS; SURFACE EXPRESSION; GAMMA-DELTA **T**-CELL **RECEPTOR** IN ACUTE BRUCELLA-MELITENSIS INFECTION)
93-8159 001 (65-KDA STRESS PROTEIN; MYCOBACTERIUM-TUBERCULOSIS DNA...

10/3,K,AB/6 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03951631 Genuine Article#: QU616 Number of References: 26
Title: **TCR**-ALPHA-CD3-DELTA-EPSILON ASSOCIATION IS THE INITIAL STEP IN ALPHA-BETA DIMER FORMATION IN MURINE T-CELLS AND IS LIMITING IN IMMATURE CD4(+)CD8(+) THYMOCYTES (Abstract Available)
Author(s): KEARSE KP; ROBERTS JL; SINGER A
Corporate Source: NCI,EXPTL IMMUNOL BRANCH,BLDG 10/BETHESDA//MD/20892
Journal: IMMUNITY, 1995, V2, N4 (APR), P391-399
ISSN: 1074-7613
Language: ENGLISH Document Type: ARTICLE
Abstract: The present study has examined the molecular events leading to formation of up dimers in normal murine thymocytes and mature T cells. We demonstrate that **TCR** assembly proceeds by initial association of **TCR** alpha with CD3 delta epsilon proteins and by association of ICRP with CD3 gamma epsilon proteins to form alpha delta epsilon and beta gamma epsilon trimers; these trimers then associate to form alpha delta epsilon-beta gamma epsilon complexes, within which alpha-beta **disulfide** bond formation occurs. We also show that **TCR** -associated protein (TRAP) associates uniquely with CD3 gamma epsilon pairs and that formation of beta gamma epsilon trimers occurs subsequent to TRAP dissociation. Importantly, we document that the assembly step that is quantitatively limiting in CD4(+)CD8(+) thymocytes is the initial association of **TCR** alpha with CD3 delta epsilon chains, which appears necessary to protect nascent **TCR**

alpha proteins from accelerated degradation within the ER of immature thymocytes.

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...Research Fronts: IMMATURE CD4+CD8+ THYMOCYTES; ADULT MURINE THYMUS; RECEPTOR OVEREXPRESSION; NEGATIVE SELECTION)
93-1602 001 (PROTEIN **FOLDING**; MOLECULAR CHAPERONES; **AGGREGATION** OF MAMMALIAN MITOCHONDRIAL MALATE-DEHYDROGENASE INVITRO)

10/3,K,AB/7 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01842119 Genuine Article#: JF804 Number of References: 31
Title: TRANSIENT **AGGREGATION** OF NASCENT THYROGLOBULIN IN THE ENDOPLASMIC-RETICULUM - RELATIONSHIP TO THE MOLECULAR CHAPERONE, BIP (Abstract Available)
Author(s): KIM PS; BOLE D; ARVAN P
Corporate Source: HARVARD UNIV,BETH ISRAEL HOSP,DIV ENDOCRINOL/BOSTON//MA/02215; HARVARD UNIV,SCH MED,CELL & DEV BIOL PROGRAM/BOSTON//MA/02115; UNIV MICHIGAN,SCH MED,DEPT BIOL CHEM/ANN ARBOR//MI/48109
Journal: JOURNAL OF CELL BIOLOGY, 1992, V118, N3 (AUG), P541-549
Language: ENGLISH Document Type: ARTICLE
Abstract: Because of its unusual length, nascent thyroglobulin (Tg) requires a long time after translocation into the endoplasmic reticulum (ER) to assume its mature tertiary structure. Thus, Tg is an ideal molecule for the study of protein **folding** and export from the ER, and is an excellent potential substrate for molecular chaperones. During the first 15 min after biosynthesis, Tg is found in transient **aggregates** with and without interchain **disulfide** bonds, which precede the formation of free monomers (and ultimately dimers) within the ER. By immunoprecipitation, newly synthesized Tg was associated with the binding protein (BiP); association was maximal at the earliest chase times. Much of the Tg released from BiP by the addition of Mg-ATP was found in **aggregates** containing interchain **disulfide** bonds; other BiP-associated Tg represented non-covalent **aggregates** and unfolded free monomers. Importantly, the immediate precursor to Tg dimer was a compact monomer which did not associate with BiP. The average stoichiometry of BiP/Tg interaction involved nearly 10 BiP molecules per Tg molecule. Cycloheximide was used to reduce the ER concentration of Tg relative to chaperones, with subsequent removal of the drug in order to rapidly restore Tg synthesis. After this treatment, nascent Tg **aggregates** were no longer detectable. The data suggest a model of **folding** of exportable proteins in which nascent polypeptides immediately upon

translocation into the ER interact with BiP. Early interaction with BiP may help in presenting nascent polypeptides to other helper molecules that catalyze **folding**, thereby preventing **aggregation** or driving **aggregate** dissolution in the ER.

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Research Fronts: 90-1310 003 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T** -CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-7788 001 (ENDOPLASMIC-RETICULUM RETENTION SIGNAL; PROTEIN **DISULFIDE** ISOMERASE; SECRETORY PATHWAY; INVARIANT CHAIN; VESICULAR STOMATITIS-VIRUS)

10/3,K,AB/8 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01820686 Genuine Article#: JE383 Number of References: 49
Title: EARLY **DISULFIDE** BOND FORMATION PREVENTS HETEROTYPIC **AGGREGATION** OF MEMBRANE-PROTEINS IN A CELL-FREE TRANSLATION SYSTEM (Abstract Available)
Author(s): YILLA M; DOYLE D; SAWYER JT
Corporate Source: SUNY BUFFALO,DEPT BIOL SCI/BUFFALO//NY/14260
Journal: JOURNAL OF CELL BIOLOGY, 1992, V118, N2 (JUL), P245-252
Language: ENGLISH Document Type: ARTICLE
Abstract: We previously demonstrated that a heterotypic complex of the two rat asialoglycoprotein receptor subunits was assembled during cell-free translation (Sawyer, J. T., and D. Doyle. 1990. Proc. Natl. Acad. Sci. USA. 87:4854-4858). We have characterized this system further by analyzing polypeptide interactions under both reducing and oxidizing translation conditions. This report shows that the complex represents a heterogeneous interaction between reduced membrane proteins rather than a specific oligomeric structure. In the reduced state membrane proteins interact in this system to form **aggregates** of diverse size and composition. The **aggregated** nascent polypeptides interact with the immunoglobulin heavy chain binding protein but this protein is not an integral component of the **aggregate**. **Aggregation** occurs via the exoplasmic domain, rather than the transmembrane domain, and the **folding** of this domain by the formation of intramolecular disulfides, prevents the interaction from occurring. Additionally, the

folded molecules containing intramolecular disulfides lack high affinity binding activity and thus appear to resemble the earliest **folding** intermediates seen in vivo (Olson, J. T., and M. D. Lane. 1989. FASEB (Fed. Am. Soc. Exp. Biol.) J. 3: 1618-1624). These results lead us to suggest that the formation of intramolecular disulfides during early biogenesis serves to prevent nonspecific associations between nascent polypeptides.

Title: EARLY **DISULFIDE** BOND FORMATION PREVENTS HETEROTYPIC **AGGREGATION** OF MEMBRANE-PROTEINS IN A CELL-FREE TRANSLATION SYSTEM
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Research Fronts: 90-1310 005 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T** -CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-1006 001 (PROTEIN **FOLDING**; SYNTHETIC PEPTIDES; HELIX COIL STABILITY-CONSTANTS FOR THE NATURALLY-OCCURRING AMINO-ACIDS)
90-1347 001...

...CYCLASE PATHWAY; HEAT-SHOCK PROTEIN HSP70 FAMILY)
90-7788 001 (ENDOPLASMIC-RETICULUM RETENTION SIGNAL; PROTEIN **DISULFIDE** ISOMERASE; SECRETORY PATHWAY; INVARIANT CHAIN; VESICULAR STOMATITIS-VIRUS)

10/3,K,AB/9 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01698903 Genuine Article#: HT965 Number of References: 40
Title: ANALYSIS OF THE GLYCOSYLATION AND PHOSPHORYLATION OF THE ALPHA-SUBUNIT OF THE LYSOSOMAL-ENZYME, BETA-HEXOSAMINIDASE-A, BY SITE-DIRECTED MUTAGENESIS (Abstract Available)
Author(s): WEITZ G; PROIA RL
Corporate Source: NIDDKD,GENET & BIOCHEM BRANCH,BLDG 10,RM 9D-15/BETHESDA//MD/20892; NIDDKD,GENET & BIOCHEM BRANCH,BLDG 10,RM 9D-15/BETHESDA//MD/20892
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1992, V267, N14 (MAY 15), P 10039-10044
Language: ENGLISH Document Type: ARTICLE
Abstract: The glycosylation and subsequent phosphorylation of mannose residues is a pivotal modification during the biosynthesis of lysosomal enzymes. We have identified the sites of N-linked glycosylation and oligosaccharide phosphorylation on the alpha-subunit of beta-hexosaminidase and have determined the influence of the oligosaccharides on the **folding** and transport of the enzyme. The potential glycosylation sequences, either singly or in combination, were eliminated through site-directed mutagenesis of the cDNA. By expression of the mutant cDNAs in COS-1 cells, each of the three glycosylation sites on the alpha-subunit was found to be modified by an oligosaccharide. One of the three oligosaccharides was the preferred site of phosphorylation. The absence of any individual oligosaccharide did not diminish the expression of the catalytic activity associated with the alpha-chain, implying proper **folding** and assembly of

subunits. A profound effect was observed, however, when all three oligosaccharides were absent. The unglycosylated alpha-subunit, resulting from genetic alteration of all three glycosylation sites or synthesis of the wild-type protein in the presence of tunicamycin, was catalytically inactive. It was found to be improperly **folded** into an insoluble **aggregate**, linked through inappropriate **disulfide** bonds. The unglycosylated protein was trapped in the lumen of the endoplasmic reticulum and was found in a complex with the Ig heavy chain-binding protein, BiP. The properties of the nonglycosylated, misfolded alpha-subunit were similar to some mutant alpha-subunits in Tay-Sachs disease patients. The results indicate that the oligosaccharides are essential, although not in a site-specific manner, for proper **folding** and cellular transport of the alpha-subunit.

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Research Fronts: 90-1310 001 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T** -CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-2081 001 (INSULIN-LIKE GROWTH FACTOR-I; CHARACTERIZATION OF...

10/3,K,AB/10 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01698461 Genuine Article#: HU423 Number of References: 72
Title: PROTEIN **FOLDING** AND PROTEIN REFOLDING (Abstract Available)
Author(s): SECKLER R; JAENICKE R
Corporate Source: UNIV REGENSBURG,INST BIOPHYS & PHYS BIOCHEM,UNIV STR 31/W-8400 REGENSBURG//GERMANY/; UNIV REGENSBURG,INST BIOPHYS & PHYS BIOCHEM,UNIV STR 31/W-8400 REGENSBURG//GERMANY/
Journal: FASEB JOURNAL, 1992, V6, N8 (MAY), P2545-2552
Language: ENGLISH Document Type: REVIEW
Abstract: The functional three-dimensional structure of proteins is determined solely by their amino acid sequences. Protein **folding** occurs spontaneously beginning with the formation of local secondary structure concomitant with a compaction of the molecule. Secondary structure elements subsequently interact to form subdomains and domains stabilized by tertiary interactions. **Disulfide** bond formation, and cis-trans isomerization of X-Pro peptide bonds, as the rate-limiting **folding** reactions, are enzymatically catalyzed during protein **folding** in the cell. Although **folding** of domains is fast enough to occur cotranslationally in vivo, such vectorial **folding** on the ribosome is not essential for attainment of the native structure of a protein. Slow steps on the pathway to the functional protein structure are docking reactions of domains,

association of subunits, or reshuffling reactions at the oligomer level. **Aggregation** as a competing side reaction is prevented, and the kinetic partition between competing polypeptide **folding** and translocation reactions is regulated by chaperone proteins binding to incompletely **folded** polypeptides.

Title: PROTEIN **FOLDING** AND PROTEIN REFOLDING
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Research Fronts: 90-1006 005 (PROTEIN **FOLDING**; SYNTHETIC PEPTIDES; HELIX COIL STABILITY-CONSTANTS FOR THE NATURALLY-OCCURRING AMINO-ACIDS)
90-0761 001 (EXPRESSION IN ESCHERICHIA-COLI; PROTEIN **FOLDING**; RECOMBINANT GENES; ACTIVE ENZYME)
90-1310 001 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T**-CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-4044 001 (PROTEIN SURFACE; MOLECULAR SHAPE; SINGLE AMINO-ACID...

10/3,K,AB/11 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

11/2/04

01667016 Genuine Article#: HR017 Number of References: 52
Title: MISFOLDING AND **AGGREGATION** OF NEWLY SYNTHESIZED PROTEINS IN THE ENDOPLASMIC-RETICULUM (Abstract Available)
Author(s): MARQUARDT T; HELENIUS A
Corporate Source: YALE UNIV,SCH MED,DEPT CELL BIOL/NEW HAVEN//CT/06510
Journal: JOURNAL OF CELL BIOLOGY, 1992, V117, N3 (MAY), P505-513
Language: ENGLISH Document Type: ARTICLE
Abstract: As a part of our studies on the **folding** of glycoproteins in the ER, we analyzed the fate of viral glycoproteins that have misfolded either spontaneously or through inhibition of N-linked glycosylation. Newly synthesized Semliki Forest virus spike glycoproteins E1 and p62 and influenza hemagglutinin were studied in infected and transfected tissue culture cells. Misfolded proteins **aggregated** in < 1 min after release from polysomes and aberrant interchain **disulfide** bonds were formed immediately. When more than one protein was misfolded, mixed **aggregates** were generated. This indicated that the formation of complexes was nonspecific, random, and not restricted to products from single polysomes. The size of the **aggregates** varied from small oligomers to complexes of several million da tons. BiP was associated noncovalently with the **aggregates** and with some of the nonaggregated products. We conclude that **aggregation** reflects the poor solubility of incompletely **folded** polypeptide chains.

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Research Fronts: 90-1310 003 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T** -CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-0761 001 (EXPRESSION IN ESCHERICHIA-COLI; PROTEIN **FOLDING**; RECOMBINANT GENES; ACTIVE ENZYME)
90-1006 001 (PROTEIN **FOLDING**; SYNTHETIC PEPTIDES; HELIX COIL STABILITY-CONSTANTS FOR THE NATURALLY-OCCURRING AMINO-ACIDS)
90-6592 001...

10/3,K,AB/12 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01629973 Genuine Article#: HM714 Number of References: 22
Title: THE EFFECT OF GLUCOCORTICOID ON THE SUBCELLULAR-LOCALIZATION, OLIGOMERIZATION, AND PROCESSING OF MOUSE MAMMARY-TUMOR VIRUS ENVELOPE PROTEIN PRECURSOR-PR74 (Abstract Available)
Author(s): COREY JL; STALLCUP MR
Corporate Source: UNIV SO CALIF,HLTH SCI CTR,DEPT PATHOL,HMR 301,2011 ZONAL AVE/LOS ANGELES//CA/90033; UNIV SO CALIF,HLTH SCI CTR,DEPT PATHOL,HMR 301,2011 ZONAL AVE/LOS ANGELES//CA/90033; UNIV SO CALIF,HLTH SCI CTR,DEPT BIOCHEM/LOS ANGELES//CA/90033
Journal: MOLECULAR ENDOCRINOLOGY, 1992, V6, N3 (MAR), P450-458
Language: ENGLISH Document Type: ARTICLE
Abstract: Mouse lymphoma cell line W7MG1 is stably infected with mouse mammary tumor virus and produces the viral envelope glycoprotein precursor Pr74, but the mature envelope proteins gp52 and gp33, which are derived from Pr74 by posttranslational processing, are produced only when the cells are cultured with a glucocorticoid agonist. The current study demonstrated that even when W7MG1 cells are grown with hormone, the conversion of Pr74 to gp52 and gp33 is an inefficient process in this cell line. At least 2 h of exposure to glucocorticoid were required to induce the appearance of gp52 and gp33; furthermore, Pr74 labeled in the absence of hormone was not converted to gp52 and gp33 upon subsequent addition of hormone. RNA synthesis inhibitors blocked the hormonal induction of gp52 and gp33, indicating that the hormone acts by promoting the expression of a new gene(s) required for the production of gp52 and gp33, rather than by inhibiting the expression of a gene(s) that prevents processing of Pr74. Subcellular fractionation studies demonstrated that Pr74 produced in either the presence or absence of hormone was associated primarily with the ER, whereas gp52 and gp33 were found in the Golgi and plasma membrane fractions. The Pr74 molecules from W7MG1 cells grown either with or without glucocorticoid coimmunoprecipitated with BiP/GRP78 and sedimented as **aggregates** of heterogeneous size. In contrast, Pr74 from virus-producing GR3A mouse mammary tumor cells, which process

Pr74 more efficiently, sedimented as apparent monomers, dimers, and trimers. These results suggest that the failure to produce mature mouse mammary tumor virus envelope proteins gp52 and gp33 in W7MG1 cells grown without hormone is due to improper **folding** and/or oligomerization of Pr74 and, as a result, failure of Pr74 to exit from the ER.

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Research Fronts: 90-1310 001 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T** -CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-3517 001 (REGULATED SECRETORY PATHWAY; TRANSFECTED PC12 CELLS; RENIN ...

...N-LINKED OLIGOSACCHARIDES; SECRETORY PATHWAY; GOLGI MEMBRANE)
90-7788 001 (ENDOPLASMIC-RETICULUM RETENTION SIGNAL; PROTEIN **DISULFIDE** ISOMERASE; SECRETORY PATHWAY; INVARIANT CHAIN; VESICULAR STOMATITIS-VIRUS)

10/3,K,AB/13 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01611204 Genuine Article#: HL679 Number of References: 35
Title: GROE PREVENTS THE ACCUMULATION OF EARLY **FOLDING** INTERMEDIATES OF PRE-BETA-LACTAMASE WITHOUT CHANGING THE **FOLDING** PATHWAY (Abstract Available)
Author(s): ZAHN R; PLUCKTHUN A
Corporate Source: UNIV MUNICH,GENZENTRUM,MAX PLANCK INST BIOCHEM,AM KLOPFERSPITZ/W-8033 MARTINSRIED//GERMANY/; UNIV MUNICH,GENZENTRUM,MAX PLANCK INST BIOCHEM,AM KLOPFERSPITZ/W-8033 MARTINSRIED//GERMANY/
Journal: BIOCHEMISTRY, 1992, V31, N12 (MAR 31), P3249-3255
Language: ENGLISH Document Type: ARTICLE
Abstract: In **folding** studies of pre-beta-lactamase in the presence of GroE, we investigated the pH dependence of the **folding** reaction. Two critical intermediates in the **folding** pathway were defined kinetically. I1 is an early **folding** intermediate recognized by GroE; the misfolding of I1 leads to **aggregation**, and this is prevented by GroE. A second intermediate I2 is released from GroE after ATP hydrolysis. Its pH-dependent misfolding to a nonnative form, which is not an **aggregate**, is not prevented by GroE. From these results, a model is proposed, in which the crucial role of GroE consists of allowing the change from I1 to I2 to take place in the complex. Fluorescence spectra of the pre-beta-lactamase complexed to GroE are very similar to those of the native state. The pathway of pre-beta-lactamase **folding** is not changed by GroE as evidenced by the same half-time and pH dependence of the **folding** reaction. GroE probably recognizes the signal sequence and some portion of the mature protein since mature beta-lactamase does not interact with GroE even under conditions of slow **folding**.

Title: GROE PREVENTS THE ACCUMULATION OF EARLY **FOLDING** INTERMEDIATES OF PRE-BETA-LACTAMASE WITHOUT CHANGING THE **FOLDING** PATHWAY
Abstract: In **folding** studies of pre-beta-lactamase in the presence of GroE, we investigated the pH dependence of the **folding** reaction. Two critical intermediates in the **folding** pathway were defined kinetically. I1 is an early **folding** intermediate recognized by

GroE; the misfolding of I1 leads to **aggregation**, and this is prevented by GroE. A second intermediate I2 is released from GroE after ATP hydrolysis. Its pH-dependent misfolding to a nonnative form, which is not an **aggregate**, is not prevented by GroE. From these results, a model is proposed, in which the...

...are very similar to those of the native state. The pathway of pre-beta-lactamase **folding** is not changed by GroE as evidenced by the same half-time and pH dependence of the **folding** reaction. GroE probably recognizes the signal sequence and some portion of the mature protein since mature beta-lactamase does not interact with GroE even under conditions of slow **folding**.
...Identifiers--RIBULOSE BISPHOSPHATE CARBOXYLASE; PROTEIN **DISULFIDE** -ISOMERASE; HEAT-SHOCK; ESCHERICHIA-COLI; ATP HYDROLYSIS; TRANSLOCATION; PURIFICATION; PRECURSOR; ASSOCIATION; MICROSOMES
Research Fronts: 90-1310 009 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T** -CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-1006 003 (PROTEIN **FOLDING**; SYNTHETIC PEPTIDES; HELIX COIL STABILITY-CONSTANTS FOR THE NATURALLY-OCCURRING AMINO-ACIDS)
90-0774 001...

10/3,K,AB/14 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01567578 Genuine Article#: HJ944 Number of References: 30
Title: ROLE OF ATP AND **DISULFIDE** BONDS DURING PROTEIN **FOLDING** IN THE ENDOPLASMIC-RETICULUM (Abstract Available)
Author(s): BRAAKMAN I; HELENIUS J; HELENIUS A
Corporate Source: YALE UNIV,SCH MED,DEPT CELL BIOL,333 CEDAR ST/NEW HAVEN//CT/06510
Journal: NATURE, 1992, V356, N6366 (MAR 19), P260-262
Language: ENGLISH Document Type: ARTICLE
Abstract: BEING topologically equivalent to the extracellular space, the lumen of the endoplasmic reticulum (ER) provides a unique **folding** environment for newly synthesized proteins. Unlike other compartments in the cell where **folding** occurs, the ER is oxidizing and therefore can promote the formation of disulphide bonds 1. The reducing agent dithiothreitol, when added to living cells, inhibits disulphide formation with profound effects on **folding** 2. Taking advantage of this effect, we demonstrate here that **folding** of influenza haemagglutinin is energy dependent. Metabolic energy is required to support the correct **folding** and disulphide bond formation in this well characterized viral glycoprotein, to rescue misfolded proteins from disulphide-linked **aggregates**, and to maintain the oxidized protein in its **folded** and oligomerization-competent state.

Title: ROLE OF ATP AND **DISULFIDE** BONDS DURING PROTEIN **FOLDING** IN THE ENDOPLASMIC-RETICULUM
...Abstract: equivalent to the extracellular space, the lumen of the endoplasmic reticulum (ER) provides a unique **folding** environment for newly synthesized proteins. Unlike other compartments in the cell where **folding** occurs, the ER is oxidizing and therefore can promote the formation of disulphide bonds 1...

...reducing agent dithiothreitol, when added to living cells, inhibits disulphide formation with profound effects on **folding** 2. Taking advantage of this effect, we demonstrate here that **folding** of influenza haemagglutinin is energy dependent. Metabolic energy is required to support the correct **folding** and disulphide bond formation in this well characterized viral glycoprotein, to rescue misfolded proteins from disulphide-linked **aggregates**, and to

maintain the oxidized protein in its **folded** and oligomerization-competent state.
Research Fronts: 90-1310 007 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T**-CELL **RECEPTOR** REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-1006 001 (PROTEIN **FOLDING**; SYNTHETIC PEPTIDES; HELIX COIL STABILITY-CONSTANTS FOR THE NATURALLY-OCCURRING AMINO-ACIDS)

10/3,K,AB/15 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01416555 Genuine Article#: GX507 Number of References: 93
Title: SECRETION AND INVIVO **FOLDING** OF THE FAB FRAGMENT OF THE ANTIBODY MCPC603 IN ESCHERICHIA-COLI - INFLUENCE OF DISULFIDES AND CIS-PROLINES (Abstract Available)
Author(s): SKERRA A; PLUCKTHUN A
Corporate Source: UNIV MUNICH,MAX PLANCK INST BIOCHEM,GENZENTRUM,AM KLOPFERSPITZ/W-8033 MARTINSRIED//GERMANY/; UNIV MUNICH,MAX PLANCK INST BIOCHEM,GENZENTRUM,AM KLOPFERSPITZ/W-8033 MARTINSRIED//GERMANY/
Journal: PROTEIN ENGINEERING, 1991, V4, N8 (DEC), P971-979
Language: ENGLISH Document Type: ARTICLE
Abstract: Using the well-characterized antibody McPC603 as a model, we had found that the F(v) fragment can be isolated from Escherichia coli as a functional protein in good yields, whereas the amount of the correctly **folded** F(ab) fragment of the same antibody produced under identical conditions is significantly lower. In this paper, we analyse the reasons for this difference. We found that a variety of signal sequences function in the secretion of the isolated chains of the F(ab) fragment or in the co-secretion of both chains in E. coli. The low yield of functional F(ab) fragment is not caused by inefficient expression or secretion in E. coli, but by inefficient **folding** and/or assembly in the periplasm. We compared the **folding** yields for the F(v) and the F(ab) fragment in the periplasm under various conditions. Several diagnostic framework variants were constructed and their **folding** yields measured. The results show that substitutions affecting cis-proline residues and those affecting various disulphide bonds in the protein are by themselves insufficient to dramatically change the partitioning of the **folding** pathway to the native structure, and the cause must lie in a facile **aggregation** of **folding** intermediates common to all structural variants. However, all structural variants could be obtained in native form, demonstrating the general utility of the secretory expression strategy.

Title: SECRETION AND INVIVO **FOLDING** OF THE FAB FRAGMENT OF THE ANTIBODY MCPC603 IN ESCHERICHIA-COLI - INFLUENCE OF DISULFIDES AND...
...Abstract: Escherichia coli as a functional protein in good yields, whereas the amount of the correctly **folded** F(ab) fragment of the same antibody produced under identical conditions is significantly lower. In...

...fragment is not caused by inefficient expression or secretion in E. coli, but by inefficient **folding** and/or assembly in the periplasm. We compared the **folding** yields for the F(v) and the F(ab) fragment in the periplasm under various conditions. Several diagnostic framework variants were constructed and their **folding** yields measured. The results show that substitutions affecting cis-proline residues and those affecting various...

...bonds in the protein are by themselves insufficient to dramatically change the partitioning of the **folding** pathway to the native structure, and the cause must lie in a facile **aggregation** of **folding** intermediates common to all structural variants.

However, all structural variants could be obtained in native...
...Identifiers--CHAINS; HIGH-LEVEL EXPRESSION; HUMAN GROWTH-HORMONE;
HEAVY-CHAIN; NUCLEOTIDE-SEQUENCE; BETA-LACTAMASE; ALKALINE-PHOSPHATASE;
DISULFIDE ISOMERASE; CRYSTAL-STRUCTURE
...Research Fronts: GENE FAMILIES; HEAVY-CHAIN VARIABLE REGIONS; SYSTEMIC
LUPUS-ERYTHEMATOSUS; SOMATIC MUTATION)
90-1006 003 (PROTEIN **FOLDING**; SYNTHETIC PEPTIDES; HELIX COIL
STABILITY-CONSTANTS FOR THE NATURALLY-OCCURRING AMINO-ACIDS)
90-1310 002 (HEAT-SHOCK PROTEINS; GAMMA-DELTA-**T**-CELL
RECEPTOR REPERTOIRE; MAIZE MITOCHONDRIAL CHAPERONIN HSP60)
90-2362 002 (STA58 MAJOR ANTIGEN GENE; RHODOCOCCUS-FASCIANS CLONING
VECTORS; ESCHERICHIA-COLI CHROMOSOME; PRECISE IDENTIFICATION)
90-0761 001 (EXPRESSION IN ESCHERICHIA-COLI; PROTEIN **FOLDING**;
RECOMBINANT GENES; ACTIVE ENZYME)
90-2285 001 (CARCINOEMBRYONIC ANTIGEN; EXPRESSION OF THE
PREGNANCY-SPECIFIC BETA...

...IMMUNOSUPPRESSANT FK506; LYMPHOCYTE SIGNAL TRANSDUCTION; ACTIVATION
ANTIGEN EXPRESSION; FLOW CYTOMETRIC ANALYSIS)
90-5686 001 (PROTEIN **DISULFIDE** ISOMERASE; PROLYL 4-HYDROXYLASE;
RAT GASTRIC MUCIN OCCURS IN THE ROUGH ENDOPLASMIC-RETICULUM)
?

14/3,K,AB/7 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

0010809895 BIOSIS NO.: 199799443955
Recombinant soluble **TCR** (sTCR) protect T cells from suppression:
Requirement for **aggregated**, pentameric, **disulfide**-linked
alpha-beta heterodimers of sTCR
AUTHOR: Paliwal V; Ptak W; Szczepanik M; Braswell E; Askenase P W
AUTHOR ADDRESS: Yale Univ. Sch. Med., New Haven, CT, USA**USA
JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2): pS302
1997 **1997**
CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997; 19970221
ISSN: 0091-6749
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

Recombinant soluble **TCR** (sTCR) protect T cells from suppression:
Requirement for **aggregated**, pentameric, **disulfide**-linked
alpha-beta heterodimers of sTCR
1997
...REGISTRY NUMBERS: **DISULFIDE**
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: **DISULFIDE**
MISCELLANEOUS TERMS: ...**T** CELL **RECEPTOR**;

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S3       1810   S1 AND S2
S4      37324   DETRIMENTAL
S5          0   S3 AND S4
S6     714834   FOLD?
S7        129   S3 AND S6
S8     431131   UNSTABL? OR AGGREGAT?
S9         18   S7 AND S8
S10        15   RD (unique items)
? s s3 and s8
            1810  S3
          431131  S8
     S11      48  S3 AND S8
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Processing
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        33643811  PY<=1998
     S14      23  S13 AND PY<=1998
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 14/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts.
```

7977588 94043304 PMID: 7693702

In vivo control of redox potential during protein folding catalyzed by bacterial protein disulfide-isomerase (DsbA).

Wunderlich M; Glockshuber R

Institut fur Biophysik und Physikalische Biochemie, Universitat Regensburg, Germany.

Journal of biological chemistry (UNITED STATES) Nov 25 1993, 268 (33) p24547-50, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The formation of disulfide bonds in Escherichia coli is catalyzed by periplasmic protein disulfide-isomerase (DsbA). When the alpha-amylase/trypsin inhibitor from Ragi, a protein containing five intramolecular disulfide bridges, is secreted into the periplasm of E. coli, large amounts of misfolded inhibitor with incomplete or incorrect disulfides are accumulated. Folding of the inhibitor in the periplasm is not improved when DsbA is coexpressed and cosecreted. However, an up to 14-fold increase in correctly folded inhibitor is observed by co-expression of DsbA in conjugation with the addition of reduced glutathione to the growth medium. This peptide acts as a disulfide-shuffling reagent and can pass the outer membrane of E. coli. Since the influence of DsbA on the folding yield of the inhibitor is reduced in the presence of oxidized glutathione, the in vivo function of DsbA appears to be dependent on the ratio between oxidizing and **reducing** thiol equivalents in the **periplasm**. The high stability of thiol reagents against air oxidation during growth of E. coli allows the investigation of oxidative protein folding in vivo under controlled, thiol-dependent redox conditions.

... in vivo function of DsbA appears to be dependent on the ratio between oxidizing and **reducing** thiol equivalents in the **periplasm**. The high stability of thiol reagents against air oxidation during growth of E. coli allows...

8666062 95354659 PMID: 7628442

Identification and characterization of a new disulfide isomerase-like protein (DsbD) in Escherichia coli.

Missiakas D; Schwager F; Raina S

Departement de Biochimie Medicale, Centre Medical Universitaire, Switzerland.

EMBO journal (ENGLAND) Jul 17 1995, 14 (14) p3415-24, ISSN 0261-4189 Journal Code: 8208664

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Previous studies have established that DsbA and DsbC, periplasmic proteins of Escherichia coli, are two key players involved in disulfide bond formation. A search for extragenic mutations able to compensate for the lack of dsbA function in vivo led us to the identification of a new gene, designated dsbD. Lack of DsbD protein leads to some, but not all, of the phenotypic defects observed with other dsb mutations, such as hypersensitivity to dithiothreitol and to benzylpenicillin. In addition, unlike the rest of the dsb genes, dsbD is essential for bacterial growth at temperatures above 42 degrees C. Cloning of the wild-type gene and sequencing and overexpression of the protein show that dsbD is part of an operon and encodes an inner membrane protein. A 138 amino acid subdomain of the protein was purified and shown to possess an oxido-reductase activity in vitro. Expressing this subdomain in the periplasmic space helped restore the phenotypic defects associated with a dsbD null mutation. Interestingly, this domain shares 45% identity with the portion of the eukaryotic protein disulfide isomerase carrying the active site. We further show that in dsbD mutant bacteria the dithiol active sites of DsbA and DsbC proteins are mostly oxidized, as compared with wild-type bacteria. Our results argue that DsbD generates a **reducing** source in the **periplasm**, which is required for maintaining proper redox conditions. The finding that overexpression of DsbD leads to a Dsb- phenotype, very similar to that exhibited by dsbA null mutants, is in good agreement with such a model.

... mostly oxidized, as compared with wild-type bacteria. Our results argue that DsbD generates a **reducing** source in the **periplasm**,

09009637 20302544 PMID: 10841975
Periplasmic protein thiol:disulfide oxidoreductases of Escherichia coli.
Fabianek R A; Hennecke H; Thony-Meyer L
Institute of Microbiology, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092, Zurich, Switzerland.
FEMS microbiology reviews (NETHERLANDS) Jul 2000, 24 (3) p303-16, ISSN 0168-6445 Journal Code: 8902526
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Disulfide bond formation is part of the folding pathway for many periplasmic and outer membrane proteins that contain structural disulfide bonds. In Escherichia coli, a broad variety of periplasmic protein thiol:disulfide oxidoreductases have been identified in recent years, which substantially contribute to this pathway. Like the well-known cytoplasmic thioredoxins and glutaredoxins, these periplasmic protein thiol:disulfide oxidoreductases contain the conserved C-X-X-C motif in their active site. Most of them have a domain that displays the thioredoxin-like fold. In contrast to the cytoplasmic system, which consists exclusively of reducing proteins, the periplasmic oxidoreductases have either an oxidising, a reducing or an isomerisation activity. Apart from understanding their physiological role, it is of interest to learn how these proteins interact with their target molecules and how they are recycled as electron donors or acceptors. This review reflects the recently made efforts to elucidate the sources of oxidising and **reducing** power in the **periplasm** as well as the different properties of certain periplasmic protein thiol:disulfide oxidoreductases of E. coli.

...acceptors. This review reflects the recently made efforts to elucidate the sources of oxidising and **reducing** power in the **periplasm** as well as the different properties of certain periplasmic protein thiol:disulfide oxidoreductases of E...

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? ds

Set      Items   Description
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S3        1270   S1 AND S2
S4        7293   NONREDUC?
S5           5   S1 AND S4
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S7         183   PERIPLASM(5N) REDUC?
S8         118   RD (unique items)
? s periplasm(5n)reducing
            5500  PERIPLASM
          468169  REDUCING
      S9     23  PERIPLASM(5N)REDUCING
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 10/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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03883328 Genuine Article#: QP276 Number of References: 31
Title: CONSTRUCTION OF A FUNCTIONAL **DISULFIDE**-STABILIZED **TCR** FV INDICATES THAT ANTIBODY AND **TCR** FV FRAMEWORKS ARE VERY SIMILAR IN STRUCTURE (Abstract Available)
Author(s): KURUCZ I; BRINKMANN U; LEE B; SEGAL DM; REITER Y; JUNG SH; PASTAN I
Corporate Source: NCI,DIV CANC BIOL DIAG & CTR,MOLEC BIOL LAB/BETHESDA//MD/20892; NCI,DIV CANC BIOL DIAG & CTR,EXPTL IMMUNOL BRANCH/BETHESDA//MD/20892
Journal: IMMUNITY, **1995**, V2, N3 (MAR), P281-287
ISSN: 1074-7613
Language: ENGLISH Document Type: ARTICLE
Abstract: **Disulfide**-stabilized Fvs (dsFv) are recombinant Fv fragments of antibodies in which the inherently **unstable** V-H-V-L heterodimer is stabilized by an interchain **disulfide** bond engineered between structurally conserved framework positions. We now design and produce a **disulfide**-stabilized Fv of a **T** cell **receptor**. It is composed of V alpha and V beta variable domains of the 2B4 **TCR** stabilized by a **disulfide** bond between framework residues of the **TCR** Fv at a site corresponding to that used for **disulfide** stabilization of antibody Fvs. For ease of production and detection, the TCRdsFv was fused to a truncated form of Pseudomonas exotoxin (PE38). The **TCR**(dsFv) retains its native conformation and is much more stable than a **TcR** scFv. Moreover, it is functional in biological assays. Because successful **disulfide** stabilization of the **TCR** Fv by the positions used for antibody Fv stabilization would not occur unless the mutated residues in **TCR** Fv are at positions closely similar to those in antibody Fvs, most likely within less than 1.5 Angstrom, these results provide very strong experimental evidence for the structural similarity between immunoglobulin and **TCR** antigen-binding variable domains.

Title: CONSTRUCTION OF A FUNCTIONAL **DISULFIDE**-STABILIZED **TCR** FV INDICATES THAT ANTIBODY AND **TCR** FV FRAMEWORKS ARE VERY SIMILAR IN STRUCTURE
, **1995**

1/21/04

A GENERAL-METHOD FOR FACILITATING HETERODIMERIC PAIRING BETWEEN 2 PROTEINS - APPLICATION TO EXPRESSION OF ALPHA-T-CELL AND BETA-**T-CELL RECEPTOR** EXTRACELLULAR SEGMENTS (Abstract Available)

Author(s): CHANG HC; BAO ZZ; YAO Y; TSE AGD; GOYARTS EC; MADSEN M; KAWASAKI E; BRAUER PP; SACCHETTINI JC; NATHENSON SG; REINHERZ EL

Corporate Source: HARVARD UNIV,SCH MED,DANA FARBER CANC INST,IMMUNOBIOL LAB,44 BINNEY ST/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT MED/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT PATHOL/BOSTON//MA/02115 ; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT MICROBIOL & IMMUNOL/BRONX//NY/10461; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT BIOCHEM/BRONX//NY/10461; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT CELLBIOL/BRONX//NY/10461; PROCEPT INC/CAMBRIDGE//MA/02139

Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **1994**, V91, N24 (NOV 22), P11408-11412

ISSN: 0027-8424

Language: ENGLISH Document Type: ARTICLE

Abstract: Generation of **soluble T-cell receptor** (TCR) molecules by a variety of genetic engineering methods has been hampered by inefficient pairing of alpha and beta subunits in the absence of their respective transmembrane regions and associated CD3 components. To overcome this obstacle, we have added 30-amino acid-long segments to the carboxyl termini of alpha and beta extracellular domains via a cleavable flexible linker. These peptide segments (BASE-p1 for alpha and ACID-p1 for beta) have been previously shown to selectively associate to form a stable heterodimeric coiled coil termed a leucine **zipper**. Homodimeric structures are not permitted due to electrostatic repulsion among amino acid side chains. Expression of a representative TCR-leucine **zipper** fusion protein in a baculovirus expression system results in production of alpha beta TCR heterodimer at 0.6-1.4 mg/liter. This yield is 5- to 10-fold greater than that of the TCR expressed in the absence of the synthetic leucine **zipper** sequence. The structure of the TCR component of the fusion heterodimer was judged to be native when probed with a panel of 17 mAbs specific for alpha and beta constant and variable domains. A mAb specific for the isolated BASE-p1/ACID-p1 coiled coil was also generated and shown to react with the TCR fusion protein. The above technology should be broadly useful in the efficient production and purification of TCRs as well as other heterodimeric proteins.

...Title: FACILITATING HETERODIMERIC PAIRING BETWEEN 2 PROTEINS - APPLICATION TO EXPRESSION OF ALPHA-T-CELL AND BETA-**T-CELL RECEPTOR** EXTRACELLULAR SEGMENTS
, **1994**

Abstract: Generation of **soluble T-cell receptor** (TCR) molecules by a variety of genetic engineering methods has been hampered by inefficient pairing...

...previously shown to selectively associate to form a stable heterodimeric coiled coil termed a leucine **zipper**. Homodimeric structures are not permitted due to electrostatic repulsion among amino acid side chains. Expression of a representative TCR-leucine **zipper** fusion protein in a baculovirus expression system results in production of alpha beta TCR heterodimer...

...fold greater than that of the TCR expressed in the absence of the synthetic leucine **zipper** sequence. The structure of the TCR component of the fusion heterodimer was judged to be...

01664046 Genuine Article#: HR186 Number of References: 23
Title: SPECIFIC LOW-AFFINITY RECOGNITION OF MAJOR HISTOCOMPATIBILITY COMPLEX PLUS PEPTIDE BY **SOLUBLE T-CELL RECEPTOR**
(Abstract Available)
Author(s): WEBER S; TRAUNECKER A; OLIVERI F; GERHARD W; KARJALAINEN K
Corporate Source: BASEL INST IMMUNOL,GRENZACHERSTR 487/CH-4005 BASEL//SWITZERLAND/; WISTAR INST/PHILADELPHIA//PA/19104
Journal: NATURE, **1992**, V356, N6372 (APR 30), P793-796
Language: ENGLISH Document Type: ARTICLE
Abstract: THE T-cell receptor is necessary and sufficient for recognition of peptides presented by major histocompatibility complex molecules 1,2. Other adhesion molecules, like CD4 or CD8, play an auxiliary role in antigen recognition by T cells 3,4. Here we analyse **T-cell receptor** (TCR) **binding** using a **soluble** rather than a cell-bound receptor molecule. A TCR-immunoglobulin chimaera is constructed with the variable and the first constant regions of both the TCR alpha- and beta-chains linked to the immunoglobulin light-chain constant regions. This soluble TCR is expressed, assembled and secreted as an alpha-beta-heterodimer by a myeloma cell line transfected with the recombinant genes. Furthermore, the soluble TCR is biologically active: it specifically inhibits antigen-dependent activation of the relevant T-cell clones and thus discriminates between proper and irrelevant peptides presented by major histocompatibility complex molecules.

Title: SPECIFIC LOW-AFFINITY RECOGNITION OF MAJOR HISTOCOMPATIBILITY COMPLEX PLUS PEPTIDE BY **SOLUBLE T-CELL RECEPTOR**
, **1992**
...Abstract: play an auxiliary role in antigen recognition by T cells 3,4. Here we analyse **T-cell receptor** (TCR) **binding** using a **soluble** rather than a cell-bound receptor molecule. A TCR-immunoglobulin chimaera is constructed with the...
Research Fronts: 90-0712 001 (T-CELL RECEPTOR; CLONAL DELETION; TRANSGENIC MICE; PERIPHERAL MECHANISMS INDUCING TISSUE TOLERANCE; **MHC** CLASS-II MOLECULES)
90-1517 001 (T-CELL RECEPTOR; CLASS-I MOLECUL

11193828 98070386 PMID: 9405420

Conformational integrity and **ligand** binding properties of a single chain T-cell receptor expressed in Escherichia coli.

Khandekar S S; Bettencourt B M; Wyss D F; Naylor J W; Brauer P P; Huestis K; Dwyer D S; Profy A T; Osburne M S; Banerji J; Jones B

Procept, Inc., Cambridge, Massachusetts 02139, USA.

Journal of biological chemistry (UNITED STATES) Dec 19 **1997**, 272 (51) p32190-7, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We recently showed that a **soluble**, heterodimeric murine D10 **T -cell receptor** (TCR) (Valpha2Calpha, Vbeta8.2Cbeta) expressed in insect cells binds both Vbeta8.2-specific bacterial superantigen staphylococcal enterotoxin C2 (SEC2) and a soluble, heterodimeric major histocompatibility complex class II I-Ak.conalbumin peptide complex with a low micromolar affinity. To define further the structural requirements for the TCR/**ligand** interactions, we have produced in Escherichia coli a soluble, functional D10 single chain (sc) TCR molecule in which the Valpha and Vbeta domains are connected by a flexible peptide linker. Purified and refolded D10 scTCR bound to SEC2 and murine major histocompatibility complex class II I-Ak.conalbumin peptide complex with thermodynamic and kinetic binding constants similar to those measured for the baculovirus-derived heterodimeric D10 TCR suggesting that neither the TCR constant domains nor potential N- or O-linked carbohydrate moieties are necessary for **ligand** recognition and for expression and proper folding of the D10 scTCR. Purified D10 scTCR remained soluble at concentrations up to 1 mM. Circular dichroism and NMR spectroscopy indicated that D10 scTCR is stabilized predominantly by beta-sheet secondary structure, consistent with its native-like conformation. Because of its limited size, high solubility, and structural integrity, purified D10 scTCR appears to be suitable for structural studies by multidimensional NMR spectroscopy.

10483985 96293497 PMID: 8692966

Covalent assembly of a **soluble T cell receptor** -peptide-major histocompatibility class I complex.

Gregoire C; Lin S Y; Mazza G; Rebai N; Luescher I F; Malissen B

Centre d'Immunologic, Institut National de la Sante et de la Recherche Medicale, Marseille, France.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jul 9 **1996**, 93 (14) p7184-9, ISSN 0027-8424 Journal Code: 7505876

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We used stepwise photochemical cross-linking for specifically assembling soluble and covalent complexes made of a T-cell antigen receptor (TCR) and a class I molecule of the major histocompatibility complex (MHC) bound to an antigenic peptide. For that purpose, we have produced in myeloma cells a single-chain Fv construct of a TCR specific for a photoreactive H-2Kd-peptide complex. Photochemical cross-linking of this TCR single-chain Fv with a soluble form of the photoreactive H-2Kd-peptide **ligand** resulted in the formation of a ternary covalent complex. We have characterized the soluble ternary complex and showed that it reacted with antibodies specific for epitopes located either on the native TCR or on the Kd molecules. By preventing the fast dissociation kinetics observed with most T cell receptors, this approach provides a means of preparing soluble TCR-peptide-MHC complexes on large-scale levels.

Covalent assembly of a **soluble T cell receptor** -peptide-major histocompatibility class I complex.

Jul 9 **1996**,

... this TCR single-chain Fv with a soluble form of the photoreactive H-2Kd-peptide **ligand** resulted in the formation of a ternary covalent

06222397 Genuine Article#: YC950 Number of References: 58
Title: Analysis of the expression of peptide-major histocompatibility complexes using high affinity soluble divalent T cell receptors (ABSTRACT AVAILABLE)
Author(s): OHerrin SM; Lebowitz MS (REPRINT) ; Bieler JG; alRamadi BK; Utz U; Bothwell ALM; Schneck JP
Corporate Source: JOHNS HOPKINS MED INST,DEPT PATHOL, 720 RUTLAND AVE, 664 G ROSS BLDG/BALTIMORE//MD/21205 (REPRINT); JOHNS HOPKINS UNIV,DEPT PATHOL & MED, DIV IMMUNOPATHOL/BALTIMORE//MD/21205; YALE UNIV,SCH MED, IMMUNOBIOL SECT/NEW HAVEN//CT/06520; INST RECH CLIN MONTREAL,IMMUNOL LAB/MONTREAL/PQ H2W 1R7/CANADA/
Journal: JOURNAL OF EXPERIMENTAL MEDICINE, **1997**, V186, N8 (OCT 20), P 1333-1345
ISSN: 0022-1007 Publication date: 19971020
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021
Language: English Document Type: ARTICLE
Abstract: Understanding the regulation of cell surface expression of specific peptide-major histocompatibility complex (MHC) complexes is hindered by the lack of direct quantitative analyses of specific peptide-MHC complexes. We have developed a direct quantitative biochemical approach by engineering **soluble** divalent **T cell receptor** analogues (TCR-Ig) that have high affinity for their cognate peptide-MHC ligands. The generality of this approach was demonstrated by specific staining of peptide-pulsed cells with two different TCR-Ig complexes: one specific for the murine alloantigen 2C, and one specific for a viral peptide from human T lymphocyte virus-1 presented by human histocompatibility leukocyte antigens-A2. Further, using 2C TCR-Ig, a more detailed analysis of the interaction with cognate peptide-MHC complexes revealed several interesting findings. Soluble divalent 2C TCR-Ig detected significant changes in the level of specific antigenic-peptide MHC cell surface expression in cells treated with gamma-interferon (gamma-IFN). Interestingly, the effects of gamma-IFN on expression of specific peptide-MHC complexes recognized by 2C TCR-Ig were distinct from its effects on total H-2 L-d expression; thus, lower doses of gamma-IFN were required to increase expression of cell surface class I MHC complexes than were required for upregulation of expression of specific peptide-MHC complexes. Analysis of the binding of 2C TCR-Ig for specific peptide-MHC ligands unexpectedly revealed that the affinity of the 2C TCR-IS for the naturally occurring alloreactive, putatively, negatively selecting, complex, dEV-8-H-2 K-bm3, is very low, weaker than 71 mu M The affinity of the 2C TCR for the other naturally occurring, negatively selecting, alloreactive complex, p2Ca-H-2 L-d, is similar to 1000-fold higher. Thus, negatively selecting peptide-MHC complexes do not necessarily have intrinsically high affinity for copnate TCR. These results, uniquely revealed by this analysis, indicate the importance of using high affinity biologically relevant cognates, such as soluble divalent TCR, in furthering our understanding of immune responses.

, **1997**
...Abstract: of specific peptide-MHC complexes. We have developed a direct quantitative biochemical approach by engineering **soluble** divalent **T cell receptor** analogues (TCR-Ig) that have high affinity for their cognate peptide-MHC ligands. The generality...
...Research Fronts: MAJOR INFECTION IN MICE; TH1 CELLS; CYTOKINE THERAPY)
95-0691 001 (T-CELL COSTIMULATION; CD40 **LIGAND** EXPRESSION; INDUCTION OF ANERGY; ANTIGEN RECEPTORS; IMMUNOGLOBULIN SUPERFAMILY; CTLA4IG IN-VITRO)
95-1368 001 (POSITIVE...

12/3,K,AB/9 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

7/3,K,AB/6 (Item 2 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

0010804336 BIOSIS NO.: 199799438396
Expression of **soluble** T-cell: Leucine **zipper** fusions
AUTHOR: Jakobsen Bent (Reprint); Gao Fu; Wilcox Ben; Wyer Jessica R; Vessey S J Rupert; O'Callaghan Christopher; Bell John I
AUTHOR ADDRESS: Mol. Immunol. Group, Inst. Mol. Med., Oxford Univ., John Radcliffe Hosp., Headington, Oxford OX9 3DU, UK**UK
JOURNAL: Immunotechnology (Amsterdam) 2 (4): p309 1996 **1996**
CONFERENCE/MEETING: 1996 Keystone Meeting on Exploring and Exploiting Antibody and Ig Superfamily Combining Sites Taos, New Mexico, USA February 22-28, 1996; 19960222
ISSN: 1380-2933
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

Expression of **soluble** T-cell: Leucine **zipper** fusions
1996
DESCRIPTORS:
MISCELLANEOUS TERMS: ...LEUCINE **ZIPPER**; ...

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2004/Jan W2
         (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
  File  55:Biosis Previews(R)  1993-2004/Jan W2
         (c) 2004 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci  1990-2004/Jan W2
         (c) 2004 Inst for Sci Info
*File  34: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES 34.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
         (c) 1998 Inst for Sci Info
*File 434: New prices as of 1/1/2004 per Information Provider
request.  See HELP RATES434.
  File 340:CLAIMS(R)/US Patent  1950-03/Jan 15
         (c) 2004 IFI/CLAIMS(R)
*File 340: Enter HELP NEWS340 & HELP ALERTS340 for search,
 display & Alert information.

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Processing
         4708001  T
         4968853  CELL
         2058509  RECEPTOR??
      S1   77197  T(W)CELL(W)RECEPTOR??
? s zipper
      S2   19632  ZIPPER
? s s1 and s2
           77197  S1
           19632  S2
      S3     185  S1 AND S2
? s s3 and py<=1998
Processing
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        33643774  PY<=1998
      S4     158  S3 AND PY<=1998
? s soluble
      S5  418046  SOLUBLE
? s s4 and s5
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          418046  S5
      S6      26  S4 AND S5
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>>>Records from unsupported files will be retained in the RD set.
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      S7      19  RD (unique items)
? t s7/3,k,ab/1-19

 7/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

11534993   98426238   PMID: 9751750
  Expression and crystallization of the complex of HLA-DR2 (DRA, DRB1*1501)
and an immunodominant peptide of human myelin basic protein.
  Gauthier L; Smith K J; Pyrdol J; Kalandadze A; Strominger J L; Wiley D C;
Wucherpfennig K W
  Department  of  Cancer  Immunology  & AIDS, Dana-Farber Cancer Institute,
```

Boston, MA 02115, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Sep 29 **1998**, 95 (20) p11828-33, ISSN 0027-8424 Journal Code: 7505876
Contract/Grant No.: AI 42316; AI; NIAID; HD-17461; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
HLA-DR2 is associated with susceptibility to multiple sclerosis (MS). A peptide from human myelin basic protein (MBP, residues 85-99) was previously found to bind to purified HLA-DR2 (DRA, DRB1*1501) and to be recognized by human MBP-specific T cell clones. **Soluble** HLA-DR2 was expressed in the baculovirus system by replacing the hydrophobic transmembrane regions and cytoplasmic segments of DRalpha and DRbeta with leucine **zipper** dimerization domains from the transcription factors Fos and Jun. In the

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?
PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
? ds

Set     Items   Description
S1      77197   T(W)CELL(W)RECEPTOR??
S2      19632   ZIPPER
S3        185   S1 AND S2
S4        158   S3 AND PY<=1998
S5     418046   SOLUBLE
S6         26   S4 AND S5
S7         19   RD (unique items)
? s soluble(5n) (T(w)cell(w)receptor)
Processing
          418046  SOLUBLE
         4708001  T
         4968853  CELL
         1632257  RECEPTOR
      S8     245  SOLUBLE(5N) (T(W)CELL(W)RECEPTOR)
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          356655  S9
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Processing
              29  S11
        33643774  PY<=1998
     S12      19  S11 AND PY<=1998
? t s12/3,k,ab/1-19

 12/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

11548713   98440384   PMID: 9767439
  Bolus injection of aqueous antigen leads to a high density of
T-cell-receptor ligand in the spleen, transient T-cell activation and
anergy induction.
  Switzer S K; Wallner B P; Briner T J; Sunshine G H; Bourque C R; Luqman M
  ImmuLogic Pharmaceutical Corporation, Waltham, MA, USA.
  Immunology (ENGLAND)   Aug 1998,  94  (4)  p513-22,  ISSN 0019-2805
Journal Code: 0374672
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Co
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18/3,K,AB/29 (Item 16 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01583025 Genuine Article#: HJ870 Number of References: 0
Title: STUDYING COMPLEX CELL CELL-**INTERACTIONS** VIA **SOLUBLE** MOLECULES - **T-CELL RECEPTOR**-MEDIATED RECOGNITION OF PEPTIDE **MHC**
Author(s): DAVIS MM
Corporate Source: STANFORD UNIV,MED CTR,SCH MED,HOWARD HUGHES MEDINST/STANFORD//CA/94305; STANFORD UNIV,MED CTR,SCH MED,DEPT MICROBIOL & IMMUNOL/STANFORD//CA/94305
Journal: CLINICAL CHEMISTRY, **1992**, V38, N3 (MAR), P450-451
Language: ENGLISH Document Type: ARTICLE

Title: STUDYING COMPLEX CELL CELL-**INTERACTIONS** VIA **SOLUBLE** MOLECULES - **T-CELL RECEPTOR**-MEDIATED RECOGNITION OF PEPTIDE **MHC**
, **1992**
?

03421100 Genuine Article#: PE388 Number of References: 37
Title: BLINDING OF A **SOLUBLE** ALPHA-BETA-**T-CELL**
RECEPTOR TO SUPERANTIGEN MAJOR HISTOCOMPATIBILITY COMPLEX LIGANDS
(Abstract Available)
Author(s): KAPPLER J; WHITE J; KOZONO H; CLEMENTS J; MARRACK P
Corporate Source: NATL JEWISH CTR IMMUNOL & RESP MED,HOWARD HUGHES MED INST,DEPT MED,DIV BASIC IMMUNOL/DENVER//CO/80206; UNIV COLORADO,SCH MED,DEPT IMMUNOL/DENVER//CO/80206; UNIV COLORADO,SCH MED,DEPT MED/DENVER//CO/80206; UNIV COLORADO,SCH MED,DEPT BIOCHEM BIOPHYS & GENET/DENVER//CO/80206
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **1994**, V91, N18 (AUG 30), P8462-8466
ISSN: 0027-8424
Language: ENGLISH Document Type: ARTICLE
Abstract: The genes for the alpha and beta chains of a murine T-cell receptor were truncated just prior to the portions encoding the transmembrane regions and introduced into baculovirus by recombination. Insect cells infected with the virus secreted a soluble form of the receptor that could be purified to homogeneity. This soluble receptor reacted with a set of six monoclonal antibodies originally raised to different epitopes on the natural transmembrane-region-containing receptor and bound with appropriate specificity to a cell surface complex of the human major histocompatibility complex class II molecule DR1 with the bacterial superantigen staphylococcal enterotoxin B.

Title: BLINDING OF A **SOLUBLE** ALPHA-BETA-**T-CELL**
RECEPTOR TO SUPERANTIGEN MAJOR HISTOCOMPATIBILITY COMPLEX LIGANDS
, **1994**
...Identifiers--STAPHYLOCOCCAL ENTEROTOXIN-B; MONOCLONAL-ANTIBODY; ANTIGEN RECEPTOR; V-BETA; PEPTIDE; RECOGNITION; **BINDING;** HETERODIMERS; MOLECULES; HLA-DR1
...Research Fronts: HUMAN T-CELL RECEPTOR; CLONAL DELETION; NEGATIVE SELECTION; INVIVO TOLERANCE; MLS ANTIGENS)
92-1511 002 (**MHC** CLASS-II MOLECULES; T-CELL RECEPTOR V-BETA GENE USAGE; **INTERACTION** OF ANTIGENIC PEPTIDES)
92-2667 002 (MAJOR HISTOCOMPATIBILITY COMPLEX CLASS-I MOLECULES; ANTIGEN PRESENTATION; CELLULAR...

18/3,K,AB/22 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03089190 Genuine Article#: NB718 Number of References: 57
Title: EARLY DEGENERATE SELECTION OF THYMOCYTES BY CLASS-I MAJOR HISTOCOMPATIBILITY COMPLEX (Abstract Available)
Author(s): GRASSI F; BARBIER E; CAZENAVE PA
Corporate Source: INST PASTEUR,DEPT IMMUNOL,CNRS,UA 359,UNITE IMMUNOCHIM ANALYT,25 RUE DR ROUX/F-75724 PARIS 15//FRANCE/; UNIV PARIS 06/PARIS//FRANCE/
Journal: EUROPEAN JOURNAL OF IMMUNOLOGY, **1994**, V24, N3 (MAR), P 627-634
ISSN: 0014-2980
Language: ENGLISH Document Type: ARTICLE

03457708 Genuine Article#: PG521 Number of References: 59
Title: **BINDING** OF SOLUBLE NATURAL LIGANDS TO A **SOLUBLE** HUMAN **T-CELL RECEPTOR** FRAGMENT PRODUCED IN ESCHERICHIA-COLI
(Abstract Available)
Author(s): HILYARD KL; REYBURN H; CHUNG S; BELL JI; STROMINGER JL
Corporate Source: ROCHE PROD LTD,BROADWATER RD/WELWYN GARDEN CIT AL7 3AY/HERTS/ENGLAND/; HARVARD UNIV,DEPT BIOCHEM & MOLEC BIOL/CAMBRIDGE//MA/02138; JOHN RADCLIFFE HOSP,INST MOLEC MED,MOLEC IMMUNOL GRP/OXFORD OX3 9DU//ENGLAND/
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **1994**, V91, N19 (SEP 13), P9057-9061
ISSN: 0027-8424
Language: ENGLISH Document Type: ARTICLE
Abstract: An Escherichia coli expression system has been developed to produce milligram quantities- of the variable domains of a human T-cell receptor from a cytotoxic T cell that recognizes the HLA-A2-influenza matrix peptide complex as a single polypeptide chain. The recombinant protein was purified by metal-chelate chromatography and then refolded in a redox buffer system. The refolded protein was shown to directly **bind** both Staphylococcus aureus enterotoxin B and the major histo compatibility complex protein-peptide complex using a BIAcore biosensor. Thus this preparation of a single-chain, variable-domain, T cell receptor fragment can **bind** both of its natural ligands and some of it is therefore a functional fragment of the receptor molecule.

Title: **BINDING** OF SOLUBLE NATURAL LIGANDS TO A **SOLUBLE** HUMAN **T-CELL RECEPTOR** FRAGMENT PRODUCED IN ESCHERICHIA-COLI
, **1994**
...Abstract: and then refolded in a redox buffer system. The refolded protein was shown to directly **bind** both Staphylococcus aureus enterotoxin B and the major histo compatibility complex protein-peptide complex using...

011180882 BIOSIS NO.: 199799814942
Analysis of the expression of peptide-major histocompatibility complexes using high affinity soluble divalent T cell receptors
AUTHOR: O'Herrin Sean M; Lebowitz Michael S (Reprint); Bieler Joan G; Al-Ramadi Basel K; Utz Ursula; Bothwell Alfred L M; Schneck Jonathan P
AUTHOR ADDRESS: Johns Hopkins Med. Inst., Dep. Pathol., 720 Rutland Ave., 664 G Ross Build., Baltimore, MD 21205, USA**USA
JOURNAL: Journal of Experimental Medicine 186 (8): p1333-1345 1997
1997
ISSN: 0022-1007
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Understanding the regulation of cell surface expression of specific peptide-major histocompatibility complex (**MHC**) complexes is hindered by the lack of direct quantitative analyses of specific peptide-**MHC** complexes. We have developed a direct quantitative biochemical approach by engineering **soluble** divalent **T cell receptor** analogues (TCR-Ig) that have high affinity for their cognate peptide-**MHC** ligands. The generality of this approach was demonstrated by specific staining of peptide-pulsed cells with two different TCR-Ig complexes: one specific for the murine alloantigen 2C, and one specific for a viral peptide from human T lymphocyte virus-1 presented by human histocompatibility leukocyte antigens-A2. Further, using 2C TCR-Ig, a more detailed analysis of the **interaction** with cognate peptide-**MHC** complexes revealed several interesting findings. Soluble divalent 2C TCR-Ig detected significant changes in the level of specific antigenic-peptide **MHC** cell surface expression in cells treated with gamma-interferon (gamma-IFN). Interestingly, the effects of gamma-IFN on expression of specific peptide-**MHC** complexes recognized by 2C TCR-Ig were distinct from its effects on total H-2 L-d expression; thus, lower doses of gamma-IFN were required to increase expression of cell surface class I **MHC** complexes than were required for upregulation of expression of specific peptide-**MHC** complexes. Analysis of the **binding** of 2C TCR-Ig for specific peptide-**MHC** ligands unexpectedly revealed that the affinity of the 2C TCR-Ig for the naturally occurring alloreactive, putatively, negatively selecting, complex, dEV-8-H-2 K-bm3, is very low, weaker than 71 mu-M. The affinity of the 2C TCR for the other naturally occurring, negatively selecting, alloreactive complex, p2Ca-H-2L-d, is apprx 1000-fold higher. Thus, negatively selecting peptide-**MHC** complexes do not necessarily have intrinsically high affinity for cognate TCR. These results, uniquely revealed by this analysis, indicate the importance of using high affinity biologically relevant cognates, such as soluble divalent TCR, in furthering our understanding of immune responses.

1997

ABSTRACT: Understanding the regulation of cell surface expression of specific peptide-major histocompatibility complex (**MHC**) complexes is hindered by the lack of direct quantitative analyses of specific peptide-**MHC** complexes. We have developed a direct quantitative biochemical approach by engineering **soluble** divalent **T cell receptor** analogues (TCR-Ig) that have high affinity for their cognate peptide-**MHC** ligands. The generality of this approach was demonstrated by specific staining of peptide-pulsed cells...

...histocompatibility leukocyte antigens-A2. Further, using 2C TCR-Ig, a more detailed analysis of the **interaction** with cognate peptide-**MHC** complexes revealed several interesting findings. Soluble divalent 2C TCR-Ig detected significant changes in the level of specific

antigenic-peptide **MHC** cell surface expression in cells treated with gamma-interferon (gamma-IFN). Interestingly, the effects of gamma-IFN on expression of specific peptide-**MHC** complexes recognized by 2C TCR-Ig were distinct from its effects on total H-2...

...lower doses of gamma-IFN were required to increase expression of cell surface class I **MHC** complexes than were required for upregulation of expression of specific peptide-**MHC** complexes. Analysis of the **binding** of 2C TCR-Ig for specific peptide-**MHC** ligands unexpectedly revealed that the affinity of the 2C TCR-Ig for the naturally occurring...

...alloreactive complex, p2Ca-H-2L-d, is apprx 1000-fold higher. Thus, negatively selecting peptide-**MHC** complexes do not necessarily have intrinsically high affinity for cognate TCR. These results, uniquely revealed...

18/3,K,AB/14 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

18/3,K,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07767002 93222495 PMID: 8467090
Interaction of the T cell receptor with bacterial superantigens.
Gascoigne N R
Department of Immunology, Scripps Research Institute, La Jolla, CA 92037.
Seminars in immunology (UNITED STATES) Feb **1993**, 5 (1) p13-21,
ISSN 1044-5323 Journal Code: 9009458
Contract/Grant No.: GM-39476; GM; NIGMS; GM-46134; GM; NIGMS
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Bacterial toxin superantigens **bind** to **MHC** class II molecules and activate a large proportion of T cells through a direct **interaction** with the T cell receptor (TCR). The toxin: TCR **interaction** involves specific recognition between the beta-chain variable region and the toxin. Although a complete alpha beta T cell receptor is required for activation of T cells, studies using purified **soluble T cell receptor** beta-chain have shown that it alone is sufficient for **binding** the toxin: class II complex. The regions of V beta and enterotoxin involved in the recognition have been determined.
Interaction of the T cell receptor with bacterial superantigens.
Feb **1993**,
Bacterial toxin superantigens **bind** to **MHC** class II molecules and activate a large proportion of T cells through a direct **interaction** with the T cell receptor (TCR). The toxin: TCR **interaction** involves specific recognition between the beta-chain variable region a

73608 94239529 PMID: 8183371

Binary and ternary complexes between T-cell receptor, class II **MHC** and superantigen in vitro.

Seth A; Stern L J; Ottenhoff T H; Engel I; Owen M J; Lamb J R; Klausner R D; Wiley D C

Department of Biochemistry and Molecular Biology, Harvard University, Cambridge, Massachusetts 02138.

Nature (ENGLAND) May 26 **1994**, 369 (6478) p324-7, ISSN 0028-0836 Journal Code: 0410462

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Superantigens are proteins that in association with class II major histocompatibility complex (**MHC**)-bearing cells can stimulate virtually all T cells that express particular classes of the variable beta-domains of the T-cell receptor (TCR). This mechanism of T-cell activation circumvents the usual requirement for peptide-specific **MHC** recognition. Staphylococcus aureus enterotoxin B (SEB) is a bacterial superantigen that causes food poisoning and shock. We have characterized the tertiary complex of SEB, a **soluble T-cell receptor**, and a **soluble** class II **MHC** molecule DR1, and the three binary complexes TCR-SEB, SEB-DR1, and the peptide-specific complex DR1-TCR. We report here that in each case the specificity of the **interaction** among the soluble molecules is the same as observed in biological assays. Native gel electrophoresis and plasmon resonance affinity measurements indicate that SEB-TCR complex can form in the absence of class II **MHC** and that SEB-TCR **interaction** increases the **binding** of DR1. The observation that a superantigen can form complexes with TCR in both the absence and presence of class II **MHC** may provide a mechanism for its ability to induce anergy in some circumstances and activation in others (reviewed in ref. 8).

Binary and ternary complexes between T-cell receptor, class II **MHC** and superantigen in vitro.

08604495 95293021 PMID: 7774629

Soluble mouse major histocompatibility complex class II molecules produced in Drosophila cells.

Wallny H J; Sollami G; Karjalainen K
Basel Institute for Immunology, Switzerland.

European journal of immunology (GERMANY) May **1995**, 25 (5) p1262-6, ISSN 0014-2980 Journal Code: 1273201
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

We have exploited Drosophila melanogaster Schneider cells and compatible inducible expression vectors to produce large amounts of secreted major histocompatibility complex (**MHC**) class II molecules (I-Ed). A simple two-step purification protocol was developed. In the first step, recombinant molecules were enriched using a monoclonal anti-class II antibody column followed by a nickel chelate column which further purified and concentrated the recombinant protein to several mg/ml. Characterization of the purified material indicates that the molecules are correctly assembled into alpha beta heterodimers. Further analysis shows that the recombinant **MHC** class II molecules are devoid of endogenous peptides and, therefore, homogeneous peptide/**MHC** complexes could be prepared by adding exogenous I-Ed-specific peptides at slightly acidic pH. Upon peptide addition, molecules underwent a conformational change into a more compact form revealed by gel filtration analysis. In addition, the peptide/**MHC** complexes were biologically active. As little as 10 ng of these complexes coated on plastic from a 100 ng/ml solution were sufficient to trigger antigen-specific T cell hybridomas. These **MHC** class II molecules, together with various forms of **soluble T cell receptor** (TcR) proteins, provide valuable tools to analyze the molecular details of TcR/antigen recognition.

May **1995**,
... cells and compatible inducible expression vectors to produce large

18/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10432813 96239290 PMID: 8656044
Soluble extracellular antigen-specific T cell immunoproteins.
Cone R E
Department of Pathology, University of Connecticut Health Center, Farmington, 06030-3105, USA.
Journal of leukocyte biology (UNITED STATES) May **1996**, 59 (5) p605-12, ISSN 0741-5400 Journal Code: 8405628
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Some T cells release proteins that **bind** specifically to antigens that have not been processed by antigen-specific T cell functions in immunoregulation and/or hypersensitivity. After certain immunization regimens, T cell immunoproteins specific for the immunogen rise in serum, and therefore may be an antigen-specific, humoral manifestation of the activation of some T cells during an immune response. Although non-**MHC** (major histocompatibility complex)-associated antigen is bound, soluble antigen-specific T cell immunoproteins share variable and constant region epitopes and some amino acid sequence with the T cell receptor for antigen alpha or beta chains, and their expression depends on T cell receptor structural genes. Herein, the properties of extracellular antigen-specific T cell immunoproteins are reviewed and it is suggested that these molecules are a **soluble** analogue of the **T cell receptor** for antigen and provide an amplifying element for some T cell functions.

May **1996**,
Some T cells release proteins that **bind** specifically to antigens that have not been processed by antigen-presenting cells. These soluble immunoproteins...

18/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10483985 96293497 PMID: 8692966

Covalent assembly of a **soluble T cell receptor** -peptide-major histocompatibility class I complex.

Gregoire C; Lin S Y; Mazza G; Rebai N; Luescher I F; Malissen B

Centre d'Immunologic, Institut National de la Sante et de la Recherche Medicale, Marseille, France.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jul 9 **1996**, 93 (14) p7184-9, ISSN 0027-8424 Journal Code: 7505876

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We used stepwise photochemical cross-linking for specifically assembling soluble and covalent complexes made of a T-cell antigen receptor (TCR) and a class I molecule of the major histocompatibility complex (**MHC**) bound to an antigenic peptide. For that purpose, we have produced in myeloma cells a single-chain Fv construct of a TCR specific for a photoreactive H-2Kd-peptide complex. Photochemical cross-linking of this TCR single-chain Fv with a soluble form of the photoreactive H-2Kd-peptide ligand resulted in the formation of a ternary covalent complex. We have characterized the soluble ternary complex and showed that it reacted with antibodies specific for epitopes located either on the native TCR or on the Kd molecules. By preventing the fast dissociation kinetics observed with most T cell receptors, this approach provides a means of preparing soluble TCR-peptide-**MHC** complexes on large-scale levels.

Covalent assembly of a **soluble T cell receptor** -peptide-major histocompatibility class I complex.

543711 96355329 PMID: 8702739

Expression of recombinant HLA-DR2 molecules. Replacement of the hydrophobic transmembrane region by a leucine zipper dimerization motif allows the assembly and secretion of soluble DR alpha beta heterodimers.

Kalandadze A; Galleno M; Foncerrada L; Strominger J L; Wucherpfennig K W

Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02115, USA.

Journal of biological chemistry (UNITED STATES) Aug 16 **1996**, 271 (33) p20156-62, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: CA47554; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Major histocompatibility complex (**MHC**) class II molecules are membrane-anchored heterodimers that present peptides on the surface of antigen presenting cells to T cells. Soluble HLA-DR2 molecules were expressed for structural and functional characterization of the **MHC** /peptide/T cell receptor recognition unit. The alpha and beta chains of DR2 (encoded by the DRA, DRB1*1501 genes) did not assemble in mammalian or insect cell lines when the transmembrane regions of one or both chains were truncated. The hydrophobic transmembrane regions of DRalpha and DRbeta facilitate assembly of the heterodimer and were therefore replaced by the leucine zipper dimerization motifs from the transcription factors Fos and Jun, which assemble as a soluble, tightly packed coiled coil structure. The DRalpha-Fos and DRbeta-Jun constructs were expressed in a methyltrophic yeast, Pichia pastoris, using the alpha-mating factor secretion signal to direct expression to the secretory pathway. DR alphabeta heterodimers were purified from supernatants using an antibody specific for the DR alphabeta heterodimer. Kinetic and quantitative peptide **binding** experiments demonstrated that recombinant DR2 molecules were efficiently loaded with an antigenic peptide. Soluble DR2 molecules can be used to define structural aspects of the **MHC**/peptide/T cell receptor **interaction** and to study the signals induced by **T cell receptor** recognition of **soluble** DR2.peptide complexes.

Dialog Acc No: 2791527 IFI Acc No: 9631253
Document Type: C
METHOD FOR DETECTION OR QUANTITATION OF AN ANALYTE USING AN ANALYTE DEPENDENT ENZYME ACTIVATION SYSTEM; REACTING WITH A CONJUGATE CONSISTING OF A DETECTABLY LABELED SUBSTRATE SPECIFIC FOR ENZYME SYSTEM; DEPOSITS WHEREVER RECEPTOR IS IMMOBILIZED
Inventors: Bobrow Mark N (US); Litt Gerald J (US)
Assignee: Du Pont de Nemours, E I & Co
Assignee Code: 25048 Document Type: REASSIGNED
Publication (No,Date), Applic (No,Date):
US 5583001 **19961210** US 94238186 19940504
Publication Kind: A
Calculated Expiration: 20131210
(Cited in 003 later patents)
Continuation Pub(No),Applic(No,Date): ABANDONED US 92914374 19920715
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED US 89330357 19890329; ABANDONED US 90494226 19900320
Division Pub(No),Applic(No,Date): US 5196306 US 90589719 19900928
Priority Applic(No,Date): US 94238186 19940504; US 92914374 19920715; US 89330357 19890329; US 90494226 19900320; US 90589719 19900928

Abstract: The present invention concerns a method to catalyze reporter deposition to improve detection or quantitation of an analyte in a sample by amplifying the detector signal which comprises reacting an analyte dependent enzyme activation system with a conjugate consisting of a detectably labeled substrate specific for the enzyme system, said conjugate reacts with the analyte dependent enzyme activation system to form an activated conjugate which deposits substantially wherever receptor for the activated conjugate is immobilized, said receptor not being reactive with the analyte dependent enzyme activation system. In another embodiment the invention concerns an assay for detecting or quantitating the presence or absence of an analyte in a sample using catalyzed reporter deposition to amplify the reporter signal.

Publication (No,Date), Applic (No,Date):
...**19961210**
Non-exemplary Claims: ...5. An assay according to claim 1 wherein the **detectable label** is selected from the group consisting of enzymes, radioactive isotopes, fluorogenic, chemiluminescent, or electrochemical or...
...10. An assay according to claim 1 wherein the activated conjugate in step (c) is **biotinylated** and is reacted with a detectably labeled **streptavidin**.
...

...17. An assay according to claim 13 wherein the **detectable label** is selected from the group consisting of enzymes, radioactive isotopes, fluorogenic, chemiluminescent, or electrochemical or...

...19. An assay according to claim 13 wherein the activated conjugate step (b) is **biotinylated** and is reacted with a detectably labeled **streptavidin**.

9/3,K,AB/6
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2730385 IFI Acc No: 9614951
Document Type: C

BETA 5 PROTEIN AND DNA ENCODING THE SAME; CONTACTING BIOLOGICAL SPECIMEN WITH ANTIBODY PROBE CAPABLE OF BINDING PROTEIN B5, DETECTING THE PRESENCE OF B5 BY DETERMINING WEATHER BINDING HAS OCCURED
Inventors: Hemler Martin E (US); Ramaswamy Hemavathi (US)
Assignee: Dana-Farber Cancer Institute Inc
Assignee Code: 11804
Publication (No,Date), Applic (No,Date):
US 5527679 **19960618** US 9354077 19930427
Publication Kind: A
Calculated Expiration: 20130618
Division Pub(No),Applic(No,Date): ABANDONED US 91694314 19910501
Priority Applic(No,Date): US 9354077 19930427; US 91694314 19910501

Abstract: In accordance with the present invention, a cDNA clone encoding a new human Beta subunit which was designated Beta 5 was found. Probes for this nucleotide sequence are described. In addition, the Beta 5 protein, its associated subunit and its cell distribution were characterized. In another embodiment, this invention relates to assays for detecting this protein. Beta 5 subunit was found present on carcinomas, but absent from lymphoid cells. Consequently, this protein can be used to determine the presence of carcinoma.

Publication (No,Date), Applic (No,Date):
...**19960618**
Non-exemplary Claims: ...7. An assay according to claim 5, wherein the **detectable-label** is selected from the group consisting of radioisotopes, enzymes, fluorogenic, chemiluminescent, and electrochemical materials...

...assay according to claim 5, wherein the biotin-conjugated antibody is detected by reacting the **biotinylated** complex first with **streptavidin**-horseradish peroxidase followed by reaction orthophenylenediamine...
?

Document Type: C
COMPOSITIONS AND METHODS FOR THE DETECTION, QUANTITATION AND PURIFICATION OF ANTIGEN-SPECIFIC T CELLS; STABLE MULTIMERIC COMPLEXES OF MAJOR HISTOCOMPATIBILITY PROTEINS AND SPECIFIC ANTIGENIC PEPTIDES TO BIND AND LABEL; MEDICAL DIAGNOSIS; AUTOIMMUNE DISEASE; ANTITUMOR, -CARCINOGENIC, AND ARTHRITIC AGENTS
Inventors: Altman John D (US); Davis Mark M (US); McHeyzer-Williams Michael G (US)
Assignee: Stanford, Leland Jr University Trustees
Assignee Code: 49136
Publication (No,Date), Applic (No,Date):
US 5635363 **19970603** US 95396220 19950228
Publication Kind: A
Calculated Expiration: 20150228
(Cited in 003 later patents)
Priority Applic(No,Date): US 95396220 19950228

Abstract: T cells are specifically labeled according to their antigen receptor by binding of a multimeric binding complex. The complex is prepared with major histocompatibility complex protein subunits having a homogeneous population of peptides bound in the antigen presentation site. The multimeric MHC-antigen complex forms a stable structure with T cells, thereby allowing for the labeling, identification and separation of specific T cells.

Publication (No,Date), Applic (No,Date):
...**19970603**
Non-exemplary Claims: ...method according to claim 3, wherein said modifying enzyme is BirA, said fusion protein is **biotinylated**, and said multivalent entity comprises at least one of **streptavidin** and avidin...

...5. A method according to claim 4, wherein said multimeric binding complex further comprises a **detectable label**.
...

...method according to claim 8, wherein said modifying enzyme is BirA, said fusion protein is **biotinylated**, and said multivalent entity comprises at least one of **streptavidin** and avidin...

...A method according to claim 9, wherein said multimeric binding complex further comprises a light **detectable label**.
...

...complex according to claim 14, wherein said modifying enzyme is BirA, said fusion protein is **biotinylated**, and said multivalent entity comprises at least one of **streptavidin** and avidin...

...binding complex according to claim 15, wherein said multimeric binding complex further comprises a light **detectable label**.

9/3,K,AB/4
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2803363 IFI Acc No: 9701036
Document Type: C
METHOD FOR LABELING DNA BY RING-OPENING OF PURINE BASES; DIRECTLY THROUGH A LINKING GROUP OR SUBSEQUENT DERIVITIZATION OF BLOCKING GROUP; DIAGNOSIS OF GENETIC DISORDERS
Inventors: McCabe Mead M (US)
Assignee: Miami, University of

Assignee Code: 55026
Publication (No,Date), Applic (No,Date):
US 5593829 **19970114** US 94241385 19940503
Publication Kind: A
Calculated Expiration: 20140114
(Cited in 003 later patents)
Continuation Pub(No),Applic(No,Date): ABANDONED US 91802815
19911206

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      Set  Items  Description
       ---  -----  -----------
? s biotinylat?
      S1     703  BIOTINYLAT?
? s detectable(5n) label
           16234  DETECTABLE
           21874  LABEL
      S2    2973  DETECTABLE(5N) LABEL
? s s1 and s2
             703  S1
            2973  S2
      S3      62  S1 AND S2
? s streptavidin
      S4    1178  STREPTAVIDIN
?
? s fluorescent
      S5   22747  FLUORESCENT
? s s3 and s4
              62  S3
            1178  S4
      S6      29  S3 AND S4
? s s6 and s5
              29  S6
           22747  S5
      S7       8  S6 AND S5
? s s7 and py<1998
               8  S7
         2952045  PY<1998
      S8       0  S7 AND PY<1998
? s s6 and py<1998
              29  S6
         2952045  PY<1998
      S9       6  S6 AND PY<1998
? t s9/3,k,ab/1-6

 9/3,K,AB/1
DIALOG(R)File 340:CLAIMS(R)/US Patent
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Dialog Acc No: 2919117  IFI Acc No: 9736476
Document Type: C
METHODS FOR SYNTHETIC UNRANDOMIZATION OF OLIGOMER FRAGMENTS; DETERMINATION
OF TARGET PROPERTY; BIOSYNTHESIS CYCLES
Inventors: Anderson Kevin (US); Brown-Driver Vickie (US); Bruice Thomas W
    (US); Cook Phillip Dan (US); Davis Peter (US); Ecker David J (US);
    Freier Susan M (US); Hanecak Ronnie (US); Sanghvi Yogesh S (US);
    Vickers Timothy (US); Wyatt Jacqueline (US)
Assignee: ISIS Pharmaceuticals Inc
Assignee Code: 28846
Publication (No,Date), Applic (No,Date):
US 5698391     19971216 US 94357396    19941216
Publication Kind:  A
Calculated Expiration: 20141216
Document Type: CERTIFICATE OF CORRECTION  Certificate of Correction Date:
    19990119
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED                  US
91749000     19910823;                          US 94196103     19940222
Priority Applic(No,Date): US 94357396    19941216; US 91749000    19910823;
US 94196103    19940222
Disclaimer Date: 20140222

Abstract: Methods useful for the determination of oligomers which have
specific activity for a target molecule from a pool of primarily randomly
assembled oligomers are provided. The disclosed methods involve repeated
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syntheses of increasingly simplified sets of oligomers coupled with selection procedures for determining oligomers having the highest activity. Freedom from the use of enzymes allows the application of these methods to any molecules which can be oligomerized in a controlled fashion.

Publication (No,Date), Applic (No,Date):
...**19971216**